Case Report

Diagnostic Dilemma in a Case of Clear Cell and MiT Family Translocation Renal Tumors

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Abstract

As of the overlapping clinical, radiological, and histopathological characteristics, it can be difficult to distinguish between clear cell renal cell carcinoma (ccRCC) and MiT family translocation renal cell carcinoma (tRCC). We describe a 48-year-old man who presented with right flank pain and substantial weight loss. Imaging studies showed a large right renal mass with renal vein tumor thrombus. The histopathological examination was suggestive of ccRCC, but certain characteristics were suggestive of MiT family tRCC. Molecular analysis could not be carried out because of the unavailability of the tests. Despite the complete surgical resection, the patient had rapid progression of disease with pulmonary and intracranial metastases.

Keywords: Translocation Renal Cell Carcinoma; Renal Neoplasms; Molecular Diagnostics

Introduction

Renal cell carcinoma (RCC) is a heterogeneous group of malignancies, with clear cell renal cell carcinoma (ccRCC) being the predominant form in adults.1,2 Conversely, MiT family translocation RCC (tRCC) is a rare condition, which was previously known by its occurrence in the pediatric and young adult populations but is now increasingly identified in adults.3-5,10 These malignancies result from chromosomal translocations involving MiT family transcription factors, such as TFE3 or TFEB, leading to the formation of oncogenic fusion proteins.6-10

The most significant issue in the differential diagnosis of RCC is the marked morphological similarity between ccRCC and MiT family tRCC. Both of these malignancies can have clear or eosinophilic cytoplasm, nested or papillary architecture, and varying degrees of necrosis, making histopathological differentiation impractical. In such instances, molecular confirmation by fluorescence in situ hybridization (FISH) or next-generation sequencing (NGS) may be necessary but not always feasible.

Distinguishing these types of tumors accurately is of great clinical significance, as MiT family tRCC can exhibit more aggressive clinical behavior. The current case report highlights the challenges of diagnosis in a high-grade renal malignancy that shares features of both ccRCC and MiT family tRCC, underscoring the limitations of morphology alone in the diagnosis of malignancies and the need for molecular analysis.

Case Presentation

The patient, who was 48 years of age at the time of admission and had been operating machinery at a manu-

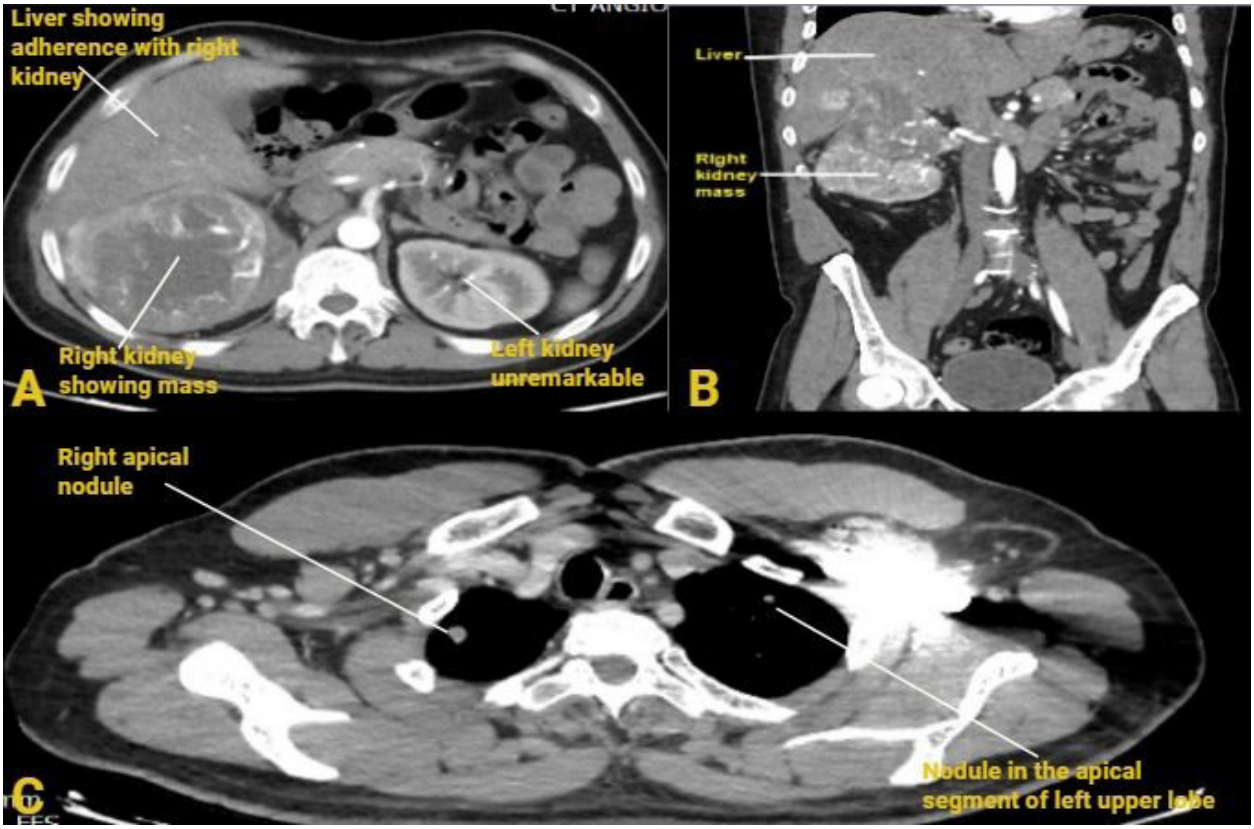

Figure 1: Contrast-enhanced computed tomography (CT) images illustrating a locally advanced right renal cell carcinoma with extension into the renal vein and evidence of pulmonary metastases.

(A) Axial contrast-enhanced CT image showing a right-renal heterogeneously enhancing mass with associated renal vein tumor thrombus and suspected hepatic interface involvement.

(B) Coronal and axial CT images illustrating the craniocaudal extent of the renal mass and the renal vein tumor thrombus.

(C) Chest CT image demonstrating newly developed pulmonary metastatic nodules, including a right apical lesion measuring 8 mm, a left upper lobe nodule measuring 5 mm, and a right upper lobe nodule measuring 4 mm.

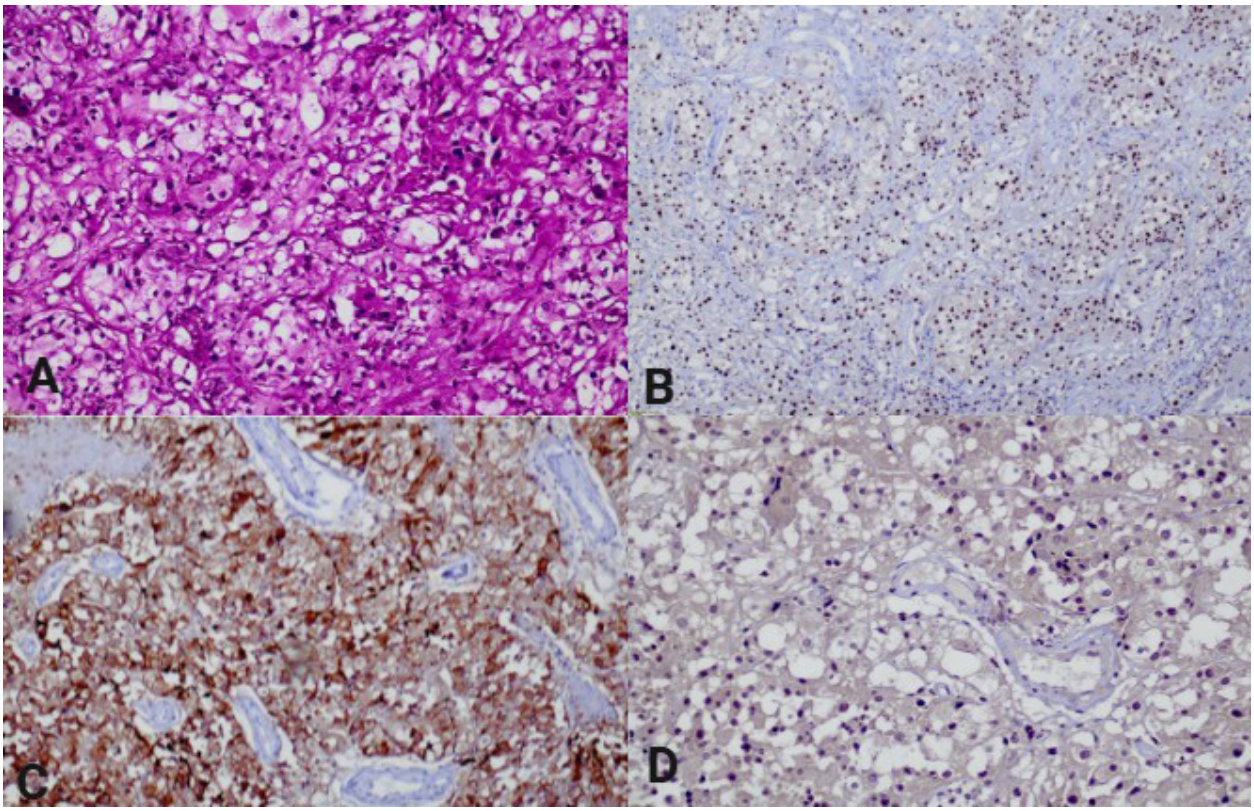

Figure 2: Histopathological and immunohistochemical features of the renal tumor.

(A) High-power photomicrograph (40×, hematoxylin and eosin) demonstrating nests of polygonal clear cells within a prominent vascular stroma.

(B) Immunohistochemistry showing strong nuclear PAX8 positivity, confirming renal epithelial origin.

(C) Carbonic anhydrase IX (CAIX) immunostaining displaying diffuse membranous expression, supporting clear cell morphology.

(D) CD10 immunostaining demonstrating apical membranous positivity in tumor cells.

facturing unit for garments, sought treatment in early 2024 with symptoms of intermittent dull and non-radiating pain in the right flank. This was associated with loss of significant weight, estimated at 15 kilograms, in the preceding six months. Other associated complaints included lack of fever, night sweats, anorexia, hematuria, and changes in bowel habits. The patient was a known diabetic with no significant medical and/or surgical history. Due to the constellation of symptoms and constitutional complaints along with flank discomfort in this healthy, middle-aged patient, there appeared to be a potential malignant pathologic process necessitating a complete diagnostic workup. On physical exam, there appeared to be a large, hard, and non-tender mass in the right flank region extending towards the midline consistent with a malignant renal mass.

Contrast-enhanced computed tomography scan of the abdomen showed a large and heterogeneously enhancing mass in the right kidney measuring approximately 15 cm in maximum diameter, along with tumor thrombus in the right renal vein. The mass showed loss of normal fat planes with surrounding hepatic surface. This made us suspect that there might be involvement of the liver. But there was no direct invasion. Additionally, there were some newly appearing pulmonary-nodules.

However, the baseline laboratory work, such as renal and liver function tests and serum electrolyte levels, was unremarkable. There were no overt biochemical changes of the paraneoplastic phenomenon, and the result can be attributed to the fact that renal cell carcinoma is commonly asymptomatic until it reaches an advanced stage. The patient subsequently underwent the right radical nephrectomy with venous thrombectomy, which was completed without intraoperative complications. The gross and microscopic findings in the nephrectomy specimen were typical of clear cell renal cell carcinoma, ISUP Grade 3, with necrosis (Fig-

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ure 2A). Nevertheless, there were some architectural and cytological features suggestive of MiT family tRCC. Immunohistochemical studies established the renal epithelial lineage, with intense nuclear reactivity for PAX8 and diffuse membranous labeling for Carbonic Anhydrase IX and CD10 (Figures 2B-D). There was no evidence of sarcomatoid or rhabdoid differentiation. Molecular confirmation by TFE3 or TFEB fluorescence in situ hybridization or immunohistochemistry was not possible on the original specimen, making diagnosis challenging. Although some architectural features suggested MiT family translocation RCC, the presence of diffuse membranous CAIX and CD10 reactivity made clear cell renal cell carcinoma the most likely diagnosis. In the absence of molecular confirmation, these findings are best classified as ccRCC with overlapping morphologic patterns rather than MiT-tRCC.

Despite negative surgical margins, follow-up imaging at three months showed rapid progression of pulmonary metastases. Adjuvant radiotherapy was subsequently implemented.

Nine months post-nephrectomy, the patient had onset seizures. Magnetic Resonance Imaging of the brain revealed a temporoparietal mass, which was excised and found to be metastatic renal cell carcinoma on histopathological examination. Additionally, the imaging revealed a recurrence in the bed post-nephrectomy. Since then, the patient has been found to benefit optimum management through an integrated and multi-disciplinary team effort of urology, radiation oncology, neurosurgery, and medical oncology on a follow-up basis. Additionally, the patient is tolerating radiotherapy and is on close follow-up. The aggressive clinical behavior of this disease, which presented early in the form of lung metastasis, central nervous system involvement, and a post-surgical recurrence, is a key determinant of the importance of a disciplined follow-through strategy in a patient with a significant risk of renal cell carcinoma.

Discussion

The current case brings into focus the challenges of diagnosis in distinguishing clear cell renal cell carcinoma from MiT family translocation renal cell carcinoma in adults. Table 1 shows how the current case fits into the spectrum of previously documented cases of MiT family RCC.

Correct subclassification of renal cell carcinoma has significant implications for treatment. Although clear cell RCC is generally treated with anti-angiogenic therapy and checkpoint inhibitors, there is emerging evidence that MiT family translocation RCC may have different therapeutic characteristics, such as sensitivity to mTOR pathway inhibitors. In the current case, the inability to make definitive subclassification limited the ability to provide specific systemic therapy. Although the patient had undergone complete surgical resection, the patient progressed rapidly with systemic disease, illustrating the aggressive course of high-grade renal malignancies of uncertain lineage. The current case illustrates the potential pitfalls of using morphology alone, which not only may impair diagnostic accuracy but also may impact treatment decisions.

Notwithstanding the traditional description of MiT family tRCC in the pediatric and young adult popula-

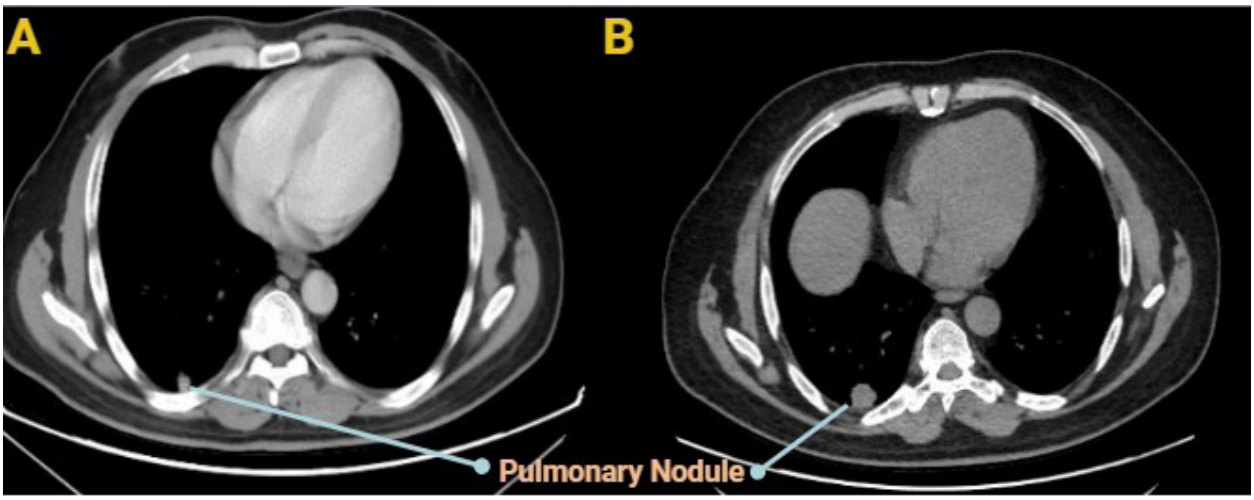

Figure 3: Interval progression of pulmonary metastatic disease on serial computed tomography.

(A–B) Sequential axial chest CT images obtained three months apart demonstrate measurable growth of multiple metastatic lung nodules. The right apical lesion increased in size from 10 mm to 26 mm, while the left apical lesion enlarged from 4.5 mm to 15 mm. A subpleural nodule in the right basal region showed interval enlargement from 13 mm to 20 mm, and an additional 8-mm nodule became evident in the right medial basal segment. Metastatic lesions are indicated by light-blue arrows.

Table 1. Comparative Clinicopathological-Profile of MiT-Family Translocation RCC: Present Case in Context of Published Literature

Parameter	Present Case	Qu et al., 202211	Prachi & Aiyer, 2021 12	Zhu et al., 202213	Wang et al., 202014	Bambury et al., 201315	Ritter-house et al., 201416	Chow et al., 202217
		Proteogenomic Series	TFE3-tRCC	TFEB-tRCC	Xp11.2 RCC	MiT-RCC	Melanotic Xp11 RCC	TFE3-tRCC
Age/Sex	48-year-old/Male	Median 34 (range 5–73); female predominance 66 (%)	52 / Male	29 / Male	38 / Male	74 / Female; 46 / Male; 33 / Female	34 / Female	20 / Male
Initial Clinical Features	Flank pain with marked involuntary weight loss (~15 kg)	Largely incidental detection; early stage in 57 (%)	Incidentally discovered renal mass	Pyrexia with incidental mass	Incidentally detected lesion	Hematuria, flank discomfort, or incidental	Incidental renal lesion	Hematuria and flank pain
Tumor Dimensions	Large mass (~15 cm), locally advanced	Wide size distribution (1.5–12 cm)	Not specified	-3.5 cm	-2.4 cm	Variable (2.6–9 cm)	Not specified	4.9 cm
Morphological Pattern	Clear cell–like morphology (ISUP grade 3) with features suspicious for MiT-tRCC	TFE3 (73 %) and TFEB (6 %) fusion tumors; ISUP grades 2–3	Papillary/alveolar growth; TFE3 IHC positive	Nested architecture with clear cytoplasm; TFEB IHC positive	Papillary pattern with psammoma bodies; TFE3 positive	Heterogeneous architectural patterns	Melanotic differentiation with sarcoid-like reaction	Mixed papillary and solid nested architecture
Molecular / Ancillary Confirmation	Definitive molecular testing unavailable	Fusion confirmation by FISH or NGS in 79 (%)	TFE3 IHC positive	TFEB IHC positive	TFE3 rearrangement confirmed by FISH	TFE3/TFEB IHC positive	TFE3 rearrangement by FISH	TFE3 IHC positive
Metastatic Behavior / Recurrence	Early pulmonary metastasis (3 mo), intracranial spread (9 mo), locoregional relapse	Advanced disease (stage III/IV) in 42 (%) at diagnosis	No metastatic disease reported	No recurrence at 8-month follow-up	Disease-free at 1 year	Lung metastasis in one reported case	No recurrence at 22 months	No recurrence at 2 years
Therapeutic Approach	Radical nephrectomy followed by radiotherapy; recurrence managed by MDT	Surgical resection ± mTOR-based systemic therapy	Radical nephrectomy	Radical nephrectomy	Partial nephrectomy	Nephrectomy; sunitinib for metastatic disease	Partial nephrectomy	Robotic nephroureterectomy
Clinical Outcome	Aggressive course with rapid progression	GP1 proteogenomic subtype associated with inferior PFS	Outcome not detailed	Favorable	Favorable	Variable, dependent on disease extent	Favorable	Favorable

Disclaimer: Cases included for comparison demonstrate the clinicopathologic spectrum of MiT family RCC; however, molecular confirmation status and tumor biology vary across reports. Abbreviations: mo = months; MDT = multidisciplinary team; ISUP = International Society of Urological Pathology; RCC = renal cell carcinoma; tRCC = translocation renal cell carcinoma; IHC = immunohistochemistry; FISH = fluorescence in situ hybridization; NGS = next-generation sequencing; PFS = progression-free survival.

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tions, there is an increasing recognition of adult-onset disease, which may potentially have an aggressive course.11,15,16 In this regard, the age of our patient (48 years) considered exclusionary but rather reflective of the expanding demographic spectrum of this entity This is particularly important from a clinical perspective, as the delayed evaluation of tRCC in adults may potentially lead to diagnostic ambiguity.

Histologically, the tumor had high-grade characteristics, including necrosis and clear to eosinophilic cytoplasm, which was largely indistinguishable from conventional ccRCC. Without the aid of molecular confirmation, such as TFE3 or TFEB rearrangement studies, it was not possible to make a definitive diagnosis. This is particularly a problem in the real-world setting, especially in institutions that lack ready access to advanced molecular studies.11,14,15

Comparison with published cases shows a high degree of heterogeneity in disease course. While some cases have been reported to have indolent disease courses after surgical treatment,13,14,17 others have shown aggressive metastatic disease, particularly in adults.15 In the current case, aggressive pulmonary metastases followed by central nervous system involvement put the patient at the aggressive end of the spectrum of reported cases. Brain metastases, although rare in tRCC and occurring in less than 5% of cases, are known to be associated with poor prognosis and were a hallmark of disease progression in the current patient.16

Recent proteogenomic studies have indicated that molecular subtypes of MiT family RCC may explain differences in tumor behavior. Qu et al. have identified a proteogenomic subtype characterized by defective DNA repair signatures and poor progression-free survival.11 Although such molecular changes cannot be verified in the current case, they provide a biologically plausible explanation for the aggressive disease course.

From a treatment perspective, the primary approach to localized disease has remained surgical excision.13,17 Nonetheless, the management of advanced or metastatic tRCC has remained inconsistent. Although mTOR inhibitors have traditionally been investigated in this context,15 recent information suggests that immune checkpoint inhibitors may have a role in the treatment of non-clear cell RCC, including those with translocation-associated pathologies. Although the current evidence is limited, these observations underscore the dynamic nature of the treatment paradigm.

Conclusion

This case highlights the challenges of diagnosis in renal tumors that exhibit overlapping morphological characteristics of ccRCC and MiT family translocation RCC. Without molecular validation, precise subtyping is difficult, especially when the clinical behavior is aggressive. The case highlights the need for molecular analysis in diagnostically challenging renal tumors and the importance of a multi-modal, multi-disciplinary approach in managing high-risk disease. It is clear that better access to molecular testing will be critical in refining classification and improving outcomes in this diverse group of renal malignancies.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. Ethical approval for publication was granted by the Institutional Review Board (IRB) of Pakistan Kidney and Liver Institute and Research Center (PKLI & RC), Lahore (IRB Reference No: PKLI-IRB/AP/00592025)

References

1. Wang Y, Suarez ER, Kastrunes G, Chen J, Li J, Zhao X, et al. Evolution of cell therapy for renal cell carcinoma. Mol Cancer. 2024;23:8. doi:10.1186/s12943-023-01911-x
2. Oliveira ACF, Noronha FB, Oliveira FLQ, Oliveira FNG, Boente LA. Renal cell carcinoma. In: de Mello RAB, editor. Medical Oncology Compendium. Academic Press; 2025. p. 457–478. doi:10.1016/B978-0-443-15609-0.00029-5
3. Ye H, Qin S, Li N, Lin M, Xu Y, Li X. A rare partner of TFE3 in Xp11 translocation renal cell carcinoma: clinicopathological analyses and detection of MED15–TFE3 fusion. Biomed Res Int. 2019;2019:5974089. doi:10.1155/2019/5974089
4. Magers MJ, Udager AM, Mehra R. MiT family translocation-associated renal cell carcinoma: a contemporary update with emphasis on morphologic, immunophenotypic, and molecular mimics. Arch Pathol Lab Med. 2015;139(10):1224–1233. doi:10.5858/arpa.2015-0196-RA
5. Martina JA, Diab HI, Li H, Puertollano R. Novel roles for the MiTF/TFE family of transcription factors in organelle biogenesis, nutrient sensing, and energy homeostasis. Cell Mol Life Sci. 2014;71(13):2483–2497. doi:10.1007/s00018-014-1565-8
6. Cutruzzula P, Cahn D, Kivlin D, Tong C, Edwards D, Amster M. A review of translocation t(6;11) renal cell carcinoma in adult patients. Curr Urol. 2017;10(2):69–71. doi:10.1159/000447154
7. Liu N, Wang Z, Gan W, Xiong L, Miao B, Chen X, et al. Renal cell carcinoma associated with Xp11.2 translocation/TFE3 gene fusions: clinical features, treatments, and prognosis. PLoS One. 2016;11(11):e0166897. doi:10.1371/journal.pone.0166897
8. Nezami BG, MacLennan GT. Clear cell renal cell carcinoma: a comprehensive review of histopathology, genetics, and differential diagnosis. Int J Surg Pathol. 2024;33(2):265–280. doi:10.1177/10668969241256111
9. Msaouel P, Genovese G, Tannir NM. Renal cell carcinoma of variant histology: biology and therapies. Hematol Oncol Clin North Am. 2023;37(5):977–992. doi:10.1016/j.hoc.2023.04.019
10. Iqbal MA, Akhtar M, Al Dayel F, Ulmer C, Paterson MC. Use of FISH analysis for diagnosis of renal cell carci-

noma subtypes. Ann Saudi Med. 1999;19(6):495–500. doi:10.5144/0256-4947.1999.495

11. Qu Y, Wu X, Anwaier A, Yang X, Li Y, Zhang C, et al. Proteogenomic characterization of MiT family translocation renal cell carcinoma. Nat Commun. 2022;13(1):7494. doi:10.1038/s41467-022-34460-w
12. Aiyer HM. MiT family translocation renal cell carcinoma in an elderly male. Indian J Pathol Microbiol. 2021 Jul 1;64(3):553–555. doi:10.4103/IJPM.IJPM_365_20
13. Zhu Y, Xia C, Ou Y, Zhang C, Li L, Yang D. TFEB-associated renal cell carcinoma: a case report and literature review. Medicine (Baltimore). 2022;101(50):e31870. doi:10.1097/MD.0000000000031870
14. Wang Y, Wang Y, Feng M, Lian X, Lei Y, Zhou H. Renal cell carcinoma associated with Xp11.2 translocation/transcription factor E3 gene fusion: an adult case report and literature review. J Int Med Res. 2020;48(10):300060520942095. doi:10.1177/0300060520942095
15. Bambury RM, Battley JE, McCarthy A, Brady C, O'Reilly S, Kelly PJ, et al. Translocation renal cell carcinomas: an evolving entity and a member of the microphthalmia transcription factor–associated family of tumors. Clin Genitourin Cancer. 2013;11(3):357–361. doi:10.1016/j.clgc.2012.12.006
16. Ritterhouse LL, Cykowski MD, Hassell LA, Slobodov G, Bane BL. Melanotic Xp11 translocation renal cancer: report of a case with a unique intratumoral sarcoid-like reaction. Diagn Pathol. 2014;9:81. doi:10.1186/1746-1596-9-81
17. Chow A, Shaker N, Parwani A. Renal cell carcinoma, MiTF/TFE3 family translocation–associated subtype. J Clin Images Med Case Rep. 2022;3(3):1717.

Authors' Contribution Statement

NBN contributed to the conception, design, acquisition, drafting of the manuscript, critical review of the manuscript, and final approval of the version to be published. AR contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. NZ contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. SM contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. SI contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. AA contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. AE contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. SMU contributed to the acquisition, analysis, interpretation of data, and drafting of the manuscript. SI contributed to the interpretation of data, drafting of the manuscript, critical review of the manuscript, and final approval of the version to be published. All authors are accountable for their work and ensure the accuracy and integrity of the study.

Conflict of Interest

Authors declared no conflict of interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.