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Eosinophilic Solid and Cystic Renal Cell Carcinoma Presenting as Bone Metastasis: A Case Report and Literature Review

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Abstract

Eosinophilic solid and cystic renal cell carcinoma (ESC-RCC) is a recently characterized renal neoplasm, typically indolent, with rare instances of metastasis. We report an 85-year-old male patient presenting with left knee pain. Magnetic resonance imaging (MRI) revealed an osteolytic lesion in the left proximal tibia. Subsequent imaging identified a primary renal mass with renal vein thrombosis. Histology showed a highly cellular infiltrative neoplasm with eosinophilic to clear cells arranged in solid sheets and papillaroid pattern. Immunohistochemistry showed diffuse positivity for PAX8, AMACR, vimentin and focal positivity for CD10 and KRT20 favouring metastatic ESC-RCC. This case underscores the potential for ESC-RCC to exhibit aggressive behavior with distant metastasis, highlighting the need for awareness of its variable clinical course and strong suspicion in evaluating KRT7 negative and KRT20 positive metastatic carcinomas.

Key words eosinophilic, solid and cystic, indolent, metastasis, case report

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Introduction

Renal tumors are heterogeneous and often challenging to classify due to overlapping histomorphologic and immunohistochemical (IHC) features. Consequently, some renal neoplasms remain unclassified. The classification of renal cell carcinomas (RCC) has evolved to include emerging and provisional entities to reduce the number of unclassified tumors [1]. The World Health Organization (WHO) recently recognized eosinophilic solid and cystic renal cell carcinoma (ESC-RCC) as a distinct subtype in the 5th edition (2022) of the WHO Classification of Urinary and Male Genital Tumors, based on its characteristic morphology and IHC profile [2].

ESC-RCC exhibits a predominantly solid and cystic architecture, with tumor cells showing abundant eosinophilic cytoplasm and granular stippling with KRT20 positivity. The most specific immunohistochemical profile of ESC-RCC includes positive staining for KRT20 and negative staining for KRT7 [3]. Although these tumors are more common in females and generally indolent, they have been reported in pediatric patients and can be multifocal or metastatic in rare cases [4]. Current literature estimates a metastasis rate of 3–5% [5]. This case report highlights

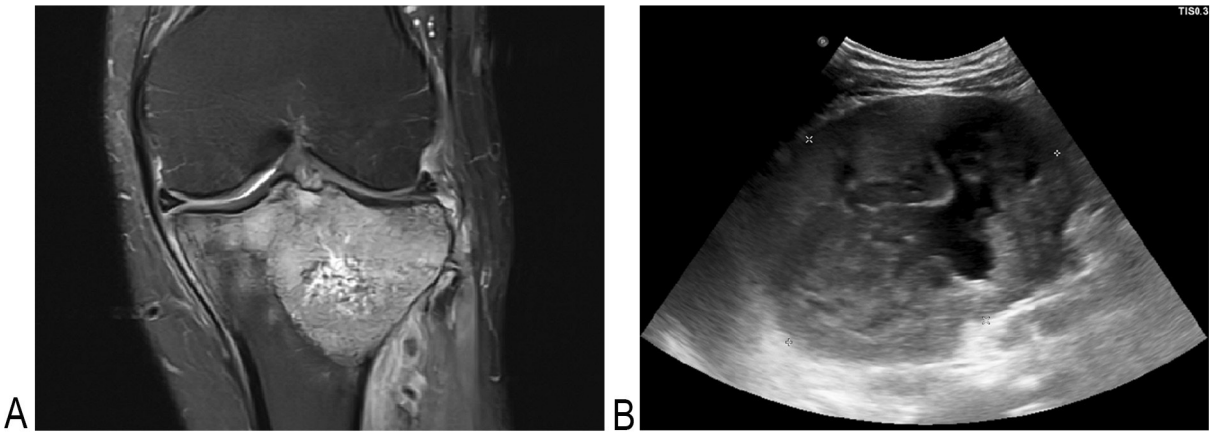

Figure 1. Imaging (A) MRI shows hyperintense lytic lesion with wide zone of transition centered in the epimetaphysis of the left proximal tibia, with surrounding soft tissue edema; (B) Ultrasonogram shows iso- to hypoechoic mass lesion in the upper pole of the left kidney with dilated pelvicalyceal system.

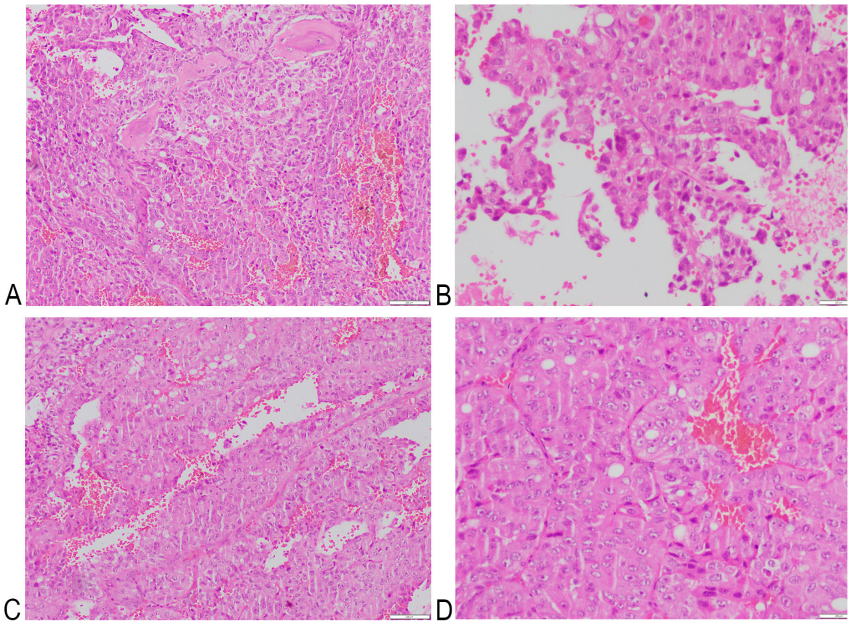

Figure 2. Histomorphology images show (A) bony fragments infiltrated by tumor cells arranged in nests (10×); (B&C) tumor cells arranged in papillary pattern (10×); (D) tumor cells with abundant eosinophilic cytoplasm, round to ovoid nuclei, prominent macronucleoli, and occasional clear vacuolated cytoplasm (40×).

a rare presentation of ESC-RCC with aggressive bone metastasis.

Case report

An 85-year-old male patient presented to the orthopedic outpatient department with left knee pain, restricted mobility, and difficulty walking. X-ray of the left knee revealed a well-defined osteolytic lesion in the lateral aspect of the left proximal tibia, without periosteal reaction. MRI showed an ill-defined lytic lesion in the proximal epi-metaphyseal region of the left tibia with a wide zone of transition, cortical thinning and a posterior cortical breach (**Figure 1A**). Differential diagnoses included metastasis, multiple myeloma, and lymphoma. A biopsy of the tibial lesion and bone marrow aspiration from the left iliac crest were performed under C-arm guidance.

Microscopic examination showed bony fragments infiltrated by a highly cellular neoplasm arranged in solid nests, sheets, glandular and papillaroid pattern (**Figure 2**). The tumor cells displayed moderate nuclear pleomorphism, have abundant eosinophilic cytoplasm, round to ovoid vesicular nuclei, and prominent macronucleoli. Intracytoplasmic vacuoles andoccasional clear cells were also seen. Mitotic figures were 2–3/10 HPF, and no necrosis was identified. These features were consistent with a metastatic poorly differentiated carcinoma. Bone marrow aspirates revealed hemodiluted smears with atypical cell clusters, suspicious for metastasis.

Initial immunohistochemistry showed focal KRT20 positivity and was negative for KRT7 and HepPar1 (**Figure 3**). Whole-body imaging was advised as part of metastatic work-up. Ultrasonogram (USG) abdomen revealed a grossly enlarged left kidney with

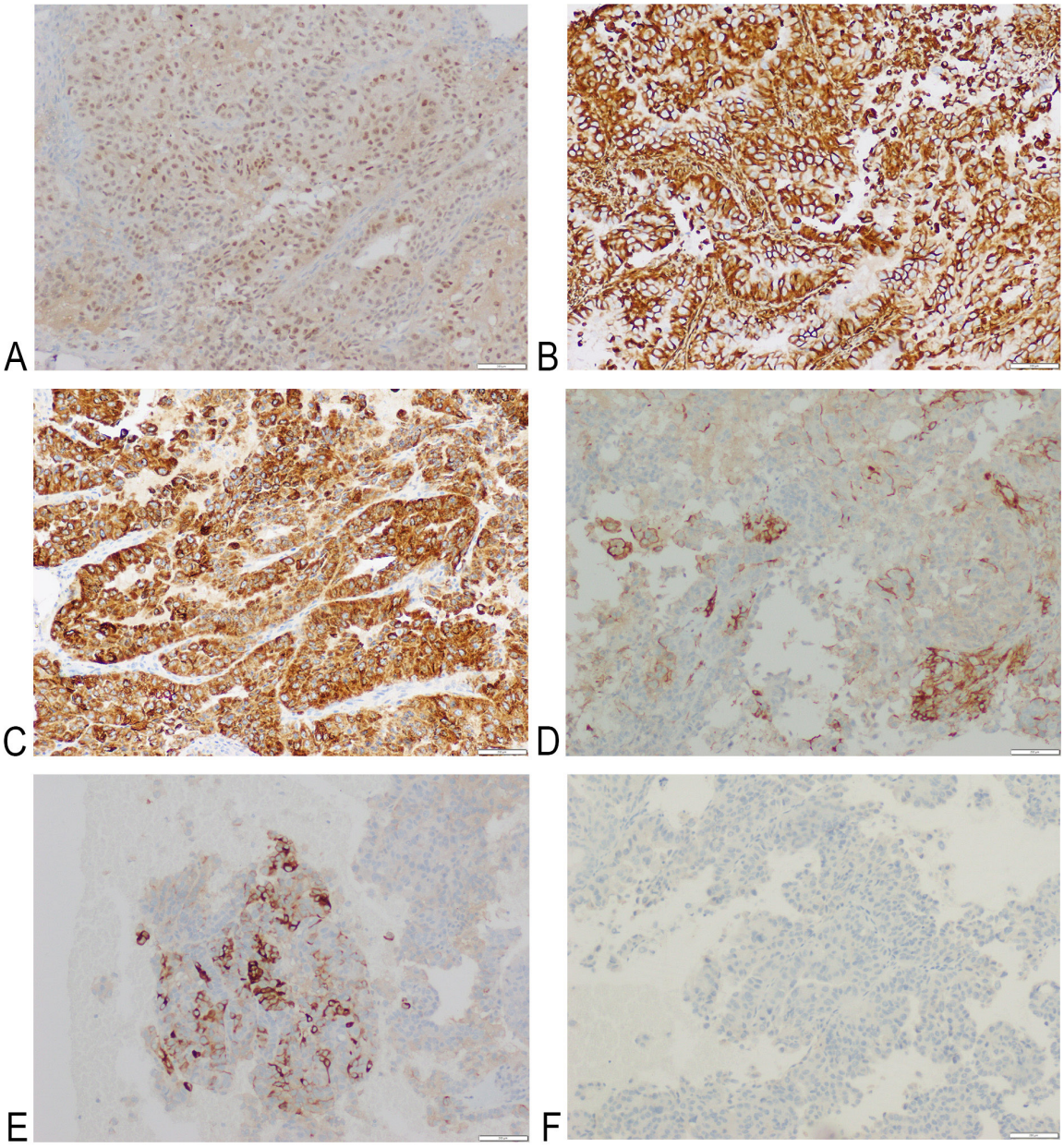

Figure 3. On immunohistochemistry, tumor cells showed diffuse positivity for (A) PAX8; (B) Vimentin; (C) AMACR; (D) focal positivity for CD10; (E) focal positivity for KRT20 and (F) negativity for HepPar1. Scale bar= 200um.

Table 1. Reported cases of ESC-RCC with distant metastasis.

Case	Age/Sex	Clinical presentation	Microscopy	Immunohistochemistry	Molecular karyotype	Site of metastasis
Our patient	85/M	Incidental finding in left knee; multifocal disease involving kidney and left proximal tibia	Abundant granular eosinophilic and focally clear cytoplasm with prominent macronucleoli and multinucleated cells	KRT20+ (focal), PAX8+, vimentin+, AMACR+, CD10(focal), KRT7–, CD117–, CAIX–, GATA3–, HMB45–	Not done	Bone metastasis
McKenney et al [11] 1st patient	15/F	Multifocal and necrotic ESC-RCC with IVC involvement and pulmonary thrombi	Classic ESC-RCC morphology	-	-	Liver metastasis
McKenney et al [11] 2nd patient	69/F	Multifocal disease involving kidneys, adrenal gland and 3 large hilar lymph nodes	Classic features with solid tumor nodules and thin septae	PAX8+, KRT20+, KRT7–	-	Hilar lymph node metastasis
Palsgrove et al [4]	Median age: 27 y (4/10 male)	5/10 multifocal tumors in young patients	Eosinophilic voluminous cytoplasm, prominent nucleoli	62.5% showed focal CathepsinK labeling	*TSC1/TSC2* mutations in all tested pediatric (8/9) and adult (6/6) cases	One patient with liver and lung metastases
Tretiakova et al [5]	50/F	Multifocal disease with involvement of left proximal humerus, pubic bone and iliac crest	Solid-cystic, eosinophilic cytoplasm with granular stippling and hobnail cells	KRT20+ (focal), PAX2+, MelanA+, CAM5.2–, KRT17-, EMA-,CD10-SMA-, HMB45–	No *TSC1/TSC2* fusions	Bone metastases (humerus, pubic bone, iliac crest)
Pathak et al [12]	45/M	Lesion in left kidney with IVC thrombus extending to infra-hepatic level	Predominantly papillary type 2 tumor composed of papillary fronds covered with eosinophilic tumor cells	KRT20+, KRT7-, CAIX-	-	Retroperitoneal lymph node,liver lesion, bone lesion in ischiopubic rami

M: Male, F: Female, IVC: Inferior Vena Cava, KRT: CytoKeratin, AMACR: Alpha Methylacyl CoA-racemase, CA IX: Carbonic Anhydrase IX, TSC: Tuberous Sclerosis Complex.

heterogeneous architecture, mild hydronephrosis, and left renal vein thrombosis with internal thrombus raising suspicion for a neoplastic etiology (**Figure 1B**).

CT imaging of the chest and abdomen showed an enlarged left kidney with loss of corticomedullary differentiation, dilated left renal vein with tumor thrombus, and suspicious perirenal lymphadenopathy.

The patient later underwent curettage with bone cementing and lateral locking compression plate (LCP) fixation of the left tibia. Histopathology of the curetted tissue showed a malignant tumor with morphology similar to the initial biopsy. Additionally, clear cells and multinucleated tumor cells were also seen. An extended IHC panel showed diffuse positivity for PAX8, AMACR, and vimentin (**Figure 3**). Occasional tumor cells were positive for CD10, while negative for SATB2, CD117, CAIX, HMB45 and GATA3.

Correlating clinical, imaging, histological, and immunohistochemical findings, a final diagnosis of metastatic eosinophilic solid and cystic renal cell carcinoma was rendered. The patient was advised adjuvant chemotherapy and immunotherapy, but he declined further treatment. He remains stable with the disease at six-month follow-up.

Discussion

Renal cell carcinoma (RCC) constitutes approximately 5% and 3% of all cancers in men and women, respectively, ranking as the sixth most common cancer in men and the tenth in women worldwide [6]. In high-income regions, incidental detection during imaging for unrelated symptoms has led to increased RCC diagnoses. Despite many tumors being small and localized, up to 17% of patients present with distant metastases at diagnosis [7].

Trpkov et al [8] first introduced the term and described Eosinophilic solid and cystic RCC as a sporadic tumor entity in patients lacking tuberous sclerosis complex (TSC). Since then, multiple cases have been documented, with an estimated prevalence of 0.07–0.2% of all RCCs [9].

ESC-RCC exhibits morphological overlap with several other eosinophilic renal neoplasms, including chromophobe RCC, oncocytoma, succinate dehydrogenase (SDH)-deficient

RCC, hybrid oncocytic tumors, thyroid-like follicular RCC, TFE3-rearranged and TFEB-altered RCCs, and epithelioid angiomyolipoma (eAML). Recent literature has documented KRT20 and MelanA expression in TFE3-rearranged/TFEB-altered RCC cases as well [10]. However, further studies with a larger study population and molecular confirmation of TFEB alterations is required to distinguish ESC-RCC from TFE3-rearranged/TFEB-altered RCCs, especially in cases with morphological overlap.

TFE3/TFEB-altered RCC was not taken into consideration as a differential since our case had typical morphology. A final diagnosis of ESC-RCC was reached after ruling out all eosinophilic renal tumors based on its typical morphology and specific immunohistochemical profile. Tretiakova et al [4] reported the first case of ESC-RCC with aggressive behavior and extensive bone metastasis, highlighting its potential for malignant progression. **Table 1** summarizes published cases of ESC-RCC with distant metastasis.

Conclusion

To conclude, our case highlights the aggressive potential of ESC-RCC, emphasizing the importance of considering this entity in the differential diagnosis of metastatic lesions with oncocytic morphology. Our case is notable for being only the sixth reported case of metastatic ESC-RCC and the third case to show bone metastasis. Unique features include an elderly male patient with a sporadic tumor and involvement of both bone and bone marrow.

Acknowledgements

None.

Ethical policy

The investigation was conducted in accordance with the Declaration of Helsinki of 1975. Written informed consent as well as consent for publication was taken from the patient.

Availability of data and materials

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Author contributions

Madhu Mitha contributed to the design, literature search and manuscript writing; Sindhu Ramamurthy contributed to the concept, manuscript editing and review; Raja Bhaskara Rajasekaran contributed to the management part of the case and manuscript editing and review; Pushpa Bhari Thippeswamy contributed to manuscript editing and review.

Competing interests

The authors declare that they have no competing interests.

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