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Case Report

Contralateral obstructive uropathy unveils eosinophilic solid and cystic renal cell carcinoma: a typical yet rare entity with rare presentation

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ABSTRACT

The World Health Organization (WHO) 2022 kidney tumour classification has introduced a novel and uncommon type of renal cell carcinoma (RCC) known as eosinophilic solid and cystic renal cell carcinoma (ESC-RCC). ESCRCC is an under-recognized, emerging new entity of sporadic renal neoplasms, with an approximate incidence of 0.2% of renal tumours. Approximately 70 cases have been reported in the literature till date. ESCRCC are usually seen in adult females, with a low stage and indolent behaviour, and rare incidence of recurrence or metastasis. They typically have solid and cystic morphology with very characteristic microscopy of abundant eosinophilic cytoplasm and prominent basophilic granules. They consistently harbor TSC1 or TSC2 mutations in tumour which is a proposed molecular marker for this entity. We presented hereby a case study in 56-year female with symptoms of contralateral obstructive uropathy for which patient underwent radiology and found out this tumour in opposite kidney. Uncommon gross presentation of extensive subcapsular haemorrhage and advanced TNM stage was noted in our case.

Keywords: Eosinophilic solid and cystic renal cell carcinoma, ESC-RCC, TSC, Obstructive uropathy, Subcapsular haemorrhage

INTRODUCTION

Eosinophilic solid cystic renal cell carcinoma (ESCRCC) is an under-recognized renal neoplasm, with morphologic features first described in 2010 in patients with tuberous sclerosis complex (TSC), and it was reported in 2016 by Trpkov et al.[1,2] The World Health Organization (WHO) 2022 renal tumor classification has collected the previous data and introduced a new and relatively uncommon type of renal cell carcinoma (RCC) known as eosinophilic solid and cystic renal cell carcinoma (ESC-RCC).[3] As it was newly introduced and the limited knowledge of approximately 70 cases in the literature, reporting this entity always remains a challenge. ESC-RCC is characterized by its indolent biological behavior and low potential for metastasis.[4] It is essential to diagnose this entity and differentiate it from other common and high-grade renal tumors. Few cases of this indolent entity are reported with distant metastasis in the literature.[5] The majority of cases occur in women and have tendency to be diagnosed at an earlier age (median age 48.5) compared to other Renal tumors.[6] We hereby presented a case of ESC RCC arising in a 56-year-old female with presenting complaints as contralateral obstructive uropathy.

CASE REPORT

A 56-year-old female with no previous medical history presented to OPD with complaints of left sided abdominal pain, fullness, vomiting on-off, nausea, weakness for 2 months. After initial physical examination she underwent multiplanar CT urography (IVU) with IV non-ionic contrast. CT scan revealed a 4.8x3.5x3.0 cm sized ill-defined lesion showing mild hyper attenuation relative to

adjacent renal parenchyma on plain scan and mild heterogenous contrast enhancing in the right kidney involving the mid and lower parts and focally extending into renal sinus. It is not visualized separately from few mid part calyces with mass effect on upper and lower calyces. Possibility of chromophobe/papillary RCC was considered.

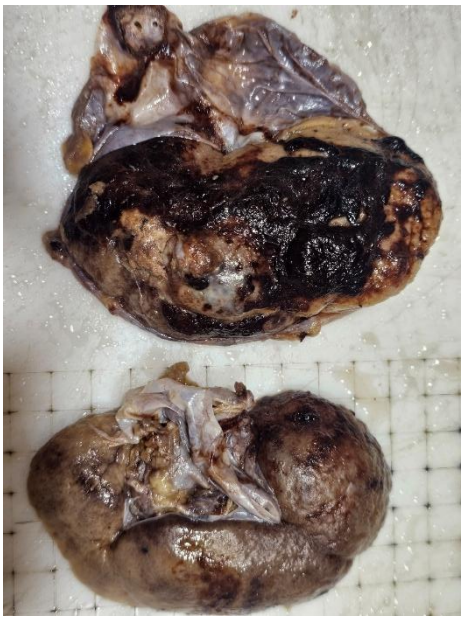

Figure 1: External surface was scarred and shows extensive subcapsular hemorrhage.

Obstructive 18.4x11.7 mm sized calculus in left renal pelvis with mild left hydronephrosis. Few nonobstructive calculi with largest 7.6x5.8 mm also noted in left kidney. Non-obstructive 9.8x5.2 mm sized calculus seen in lower part of calyx of right kidney.

Figure 2: Solid cystic mass located in middle part near hilum.

Figure 3: Friable, tan brown mass involves renal sinus fat.

Figure 4: Subcapsular nodule (arrow).

She underwent right nephrectomy with unremarkable post-operative period. On gross examination, external surface was scarred and shows extensive subcapsular hemorrhage (figure 1). Cut surface showed a solid cystic mass measuring 5x4.8x 2.5 cm located in middle part near hilum (figure 2). It was friable, tan brown and involves renal sinus fat (figure 3). Serial sections of tumor showed cystic changes involving capsule and presenting as subcapsular nodule measuring 1.0 cm (figure 4).

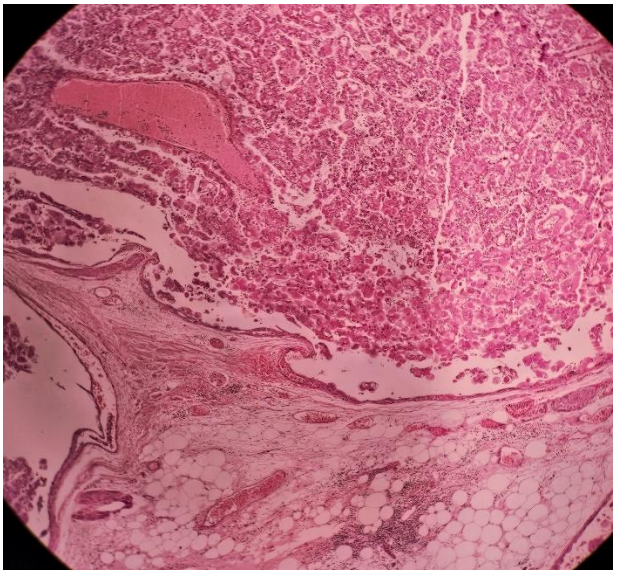

Figure 5: Solid cystic tumor involving renal sinus fat (40x).

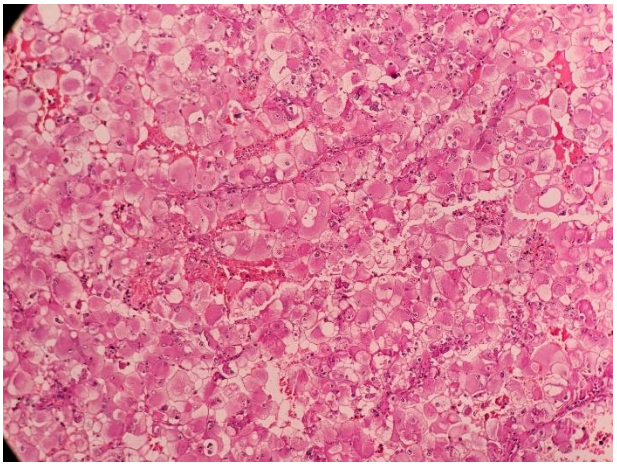

Figure 6: Polygonal tumor cells with abundant eosinophilic cytoplasm (100x).

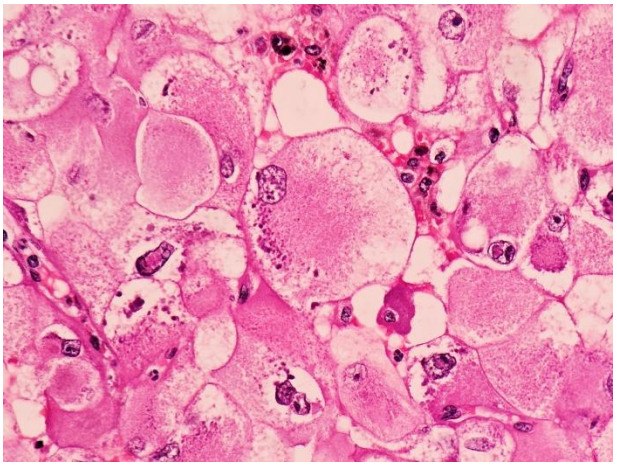

Figure 7: Coarse basophilic granular cytoplasmic stippling (400x).

Tumor was seen invading pelvicalyceal system and infiltrating capsule. No evidence of renal thrombus. Microscopically, the tumor had a solid, cystic, and occasionally papillary architecture situated near hilum involving renal sinus fat (figure 5) without involving perirenal fat.

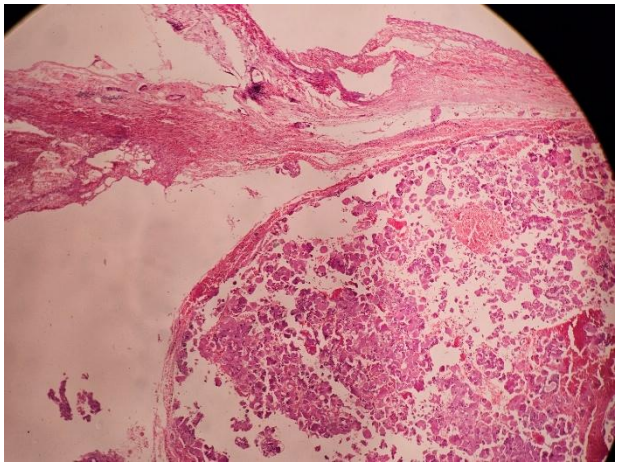

Figure 8: Capsule is involved by a small cystic nodule of tumor along with subcapsular hemorrhage (40x).

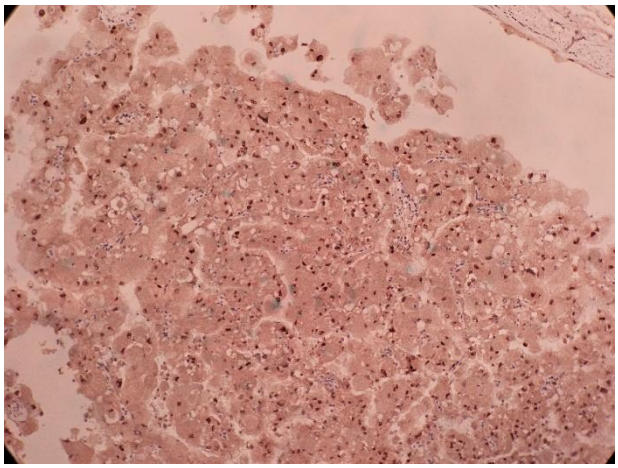

Figure 9: Tumor cells positive for PAX8 (100x).

The tumor cells were polygonal, with abundant eosinophilic cytoplasm, round to oval nuclei, moderate to severe pleomorphism, and prominent nucleoli (Figure 6) approximately equivalent to International Society of Urology Pathology (ISUP) grade 3. Intracytoplasmic vacuoles were noted at places. Many cells show prominent fine or coarse basophilic granular cytoplasmic stippling. (Figure 7). The cystic structures were lined by a single layer of cells with a “hobnail” appearance. Few clusters also showed groups of foamy macrophages centrally. significant areas of intratumoral hemorrhage along with hemosiderin pigment were noted. subcapsular hemorrhage is predominantly seen. Capsule is involved by a small cystic nodule of tumor (figure 8). Tumor necrosis, mitotic activity, and perinuclear clearing were not observed. Lymphatic and vascular invasion was not seen. The renal

parenchyma adjacent to the tumor was compressed and relatively unremarkable. Ureter showed ulcerated and inflamed transitional epithelium. The tumor cells were positive for PAX8 (figure 9), weakly and focally positive for CK20 (figure 10).

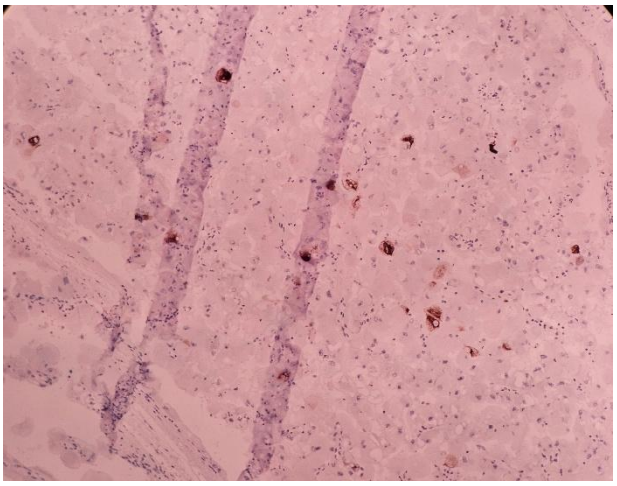

Figure 10: Tumor cells focally positive for CK20 (100x).

DISCUSSION

Trpkov et al originally suggested and described ESC RCC, a novel subtype of renal cell carcinoma, in 2016.[2] Initially, it was reported exclusively in female patients with tuberous sclerosis.[7] It has characteristic solid and cystic morphology on gross with predominantly eosinophilic tumor cells. Due to its unique morphological features and immune phenotype, it was previously misdiagnosed as an "unclassified renal cell carcinoma" or described as "unclassified eosinophilic renal tumor". In the latest fifth edition of the WHO renal tumor classification, it is classified as a morphologically defined renal tumor under some specific category. About 10% of ESC RCC cases are associated with TSC patients, but most cases are sporadic.[8] The clinical manifestations of ESC RCC are non-specific and as it remains indolent, it get discovered incidentally. ESC RCC is a biologically relatively inert, slow-growing, uncommon low-grade malignant tumor with a good prognosis. Recurrence and distant metastasis are reported rarely.[9]

The specific morphological and microscopic characteristics along with typical immunohistochemical profile of this entity give ease in diagnosing ESC-RCC. ESC-RCCs typically present as solitary, small size, and low-stage tumor, with few multifocal and bilateral cases reported in the literature and is predominantly described in women.[9] The onset age has a wide range, including pediatric patients, with an average of 57 years of age.[3] Our case reported in 56 year old women with radiology showing an ill-defined lesion 4.8x3.5x3.0 cm , extending into renal sinus in right kidney whereas her left kidney detected with large obstructive calculus. Because of its indolent nature, Clinical symptoms are quite rare. The tumor may be discovered incidentally during imaging tests conducted for other reasons totally unrelated to the tumor.[10] Our patient presented with left side abdominal pain, fullness, vomiting on off, nausea, body weakness for 2 months. Macroscopically, ESC-RCC typically presents as a well-defined, non-encapsulated tumor, grossly showing both solid and cystic areas. Grossly the usual presentation is presence of macrocysts, however few cases were also reported with only microscopic cysts.[11] Largely reported tumors had a small size, with a mean of 4.2 cm. However, tumor sizes can be variable, ranging from 1.2 to 13.5 cm in the greatest dimension, as documented by the largest series reported by Trpkov et al .[12] Our case, grossly showed scarred surface with extensive subcapsular hemorrhage, an unusual presentation. Hilar based solid cystic tan colored mass measures approx. 5 cm involving renal sinus and capsule.

Microscopically, they show diffuse acinar or nested growth, with cysts lined by hobnailed cells. Cells have voluminous eosinophilic cytoplasm, with granular stippling, and round to oval nuclei probably with WHO/ISUP grade 2-3. Some cells may also show leishmania body like coarse eosinophilic cytoplasmic granules. Intracytoplasmic vacuolization (micro or macro), insular, tubular or clear cell areas can be identified. Rarely described changes were Multinucleation, calcification, psammoma bodies.[13] Our case depicted very typical microscopy with prominent basophilic stippling and WHO/ISUP grade 3 nuclei with renal sinus and capsular involvement suggesting advanced TNM stage. Morphologic differentials for ESCRCC to be considered and should be differentiated from other high grade RCC include eosinophilic clear cell RCC (CCRCC), chromophobe RCC, oncocytomas, succinyl dehydrogenase (SDH)-deficient RCC, hybrid oncolytic RCC, and epithelioid angiomyolipoma (eAML).[13] With help of IHC panel, it is possible to distinguish all these entities. For our case, possibilities of differentials like chromophobe and papillary RCC were considered on radiology.

On immunophenotyping the tumor cells uniformly express PAX-8, and Pan-cytokeratin (AE1/AE3 and CK8/18). CK20 is characteristically seen in 74% to 80% cases, while CK7 is usually negative (focal expression seen in 31% cases). CA-IX is mostly negative (positive in CCRCC), and focal expression of CD10 and CD117 has been reported.[9-13] Loghin A et al reported in their study that the tumor cells were positive for PAX8, weakly and focally positive for CK20. (we had similar findings in our case too.)[14] ESCRCCs predominantly behaves in an indolent manner, with limited disease progression.[9] However, they can rarely show malignant features; 5% of reported cases had malignant disease with visceral (lung and liver) or lymph node metastases.[2-9] In a series comparing ESCRCC resembling epithelioid AML (eAML), 2 of 4 ESCRCC were malignant· ESCRCC is postulated to be the sporadic counterpart of TSC-associated RCC, as they consistently

harbor TSC1 or TSC2 mutations in all tumors, suggested to be a molecular marker for this tumor.[13] A study has reported TSC1 or TSC2 mutations in 8 of 9 pediatric and in all 6 adult cases of ESCRCC.[15]

CONCLUSION

ESC-RCC is a rare tumor with a unique morphology, immunohistochemical profile, and molecular characteristics, which has been clearly defined as an entity in the new WHO 2022 classification. Our case reported an unusual presentation with patient presenting as symptoms of contralateral obstructive uropathy of left kidney whereas renal mass was detected in right kidney on radiology. Although this rare entity has been reported as indolent entity in literature, our case had advanced TNM stage along with extensive subcapsular hemorrhage. Pathologists should be aware of this typical yet rare and relatively under-recognized entity so that this indolent tumor will have better patient outcomes.

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