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Case Report

Eosinophilic Solid and Cystic Renal Cell Carcinoma; a Case Report in an Elderly Male

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Abstract

Eosinophilic Solid and Cystic Renal Cell Carcinoma (ESC- RCC) was first described by Trpkov *et al.*, as a novel entity of renal neoplasms with characteristic clinical, pathological and molecular features. ESC-RCC has female predominance with few cases reported in males. Herein, we report the first case of ESC-RCC is an elderly male patient.

Keywords: Renal Cell Carcinoma (RCC); Eosinophilic; solid and cystic renal cell carcinoma (ESC-RCC); Tuberous Sclerosis; Emerging entity; Kidney.

INTRODUCTION

Eosinophilic solid and cystic renal cell carcinoma (ESC-RCC) has been recently described as an emerging subtype of renal cell carcinoma with indolent behaviour. Many reported cases show somatic loss of function mutations in TSC1 or TSC2 in these tumors [1]. Although this neoplasm is mainly described in adult females, there are few reports in male patients [1, 2]. However, none of the documented cases occurred in men aged more than 65 years.

CASE REPORT

A 67-year-old male patient, not known to have Tuberous Sclerosis or family history of cancers, referred to our hospital as a case of incidentally found right renal mass discovered on abdominal Magnetic Resonance Imaging. He had no history of haematuria or weight loss. The patient was an ex-smoker for 30 years. He underwent a computed tomography scan study (CT scan) of the chest, abdomen and pelvis, and showed a right kidney lower pole heterogeneous exophytic mass with minimal cystic changes. The mass measured 4 x 2.5 cm with enhancement following intravenous contrast. The mass had no extension into the right renal sinus fat. The renal vein was patent. The patient underwent partial nephrectomy procedure to preserve as much as possible of his kidney parenchyma.

Gross examination of the specimen revealed a well-circumscribed, tan-brown, partially cystic mass that measured 4 x 2.5 x 2 cm (Figure 1).

Histological assessment of the mass revealed a tumor composed of cells arranged in solid, compact nests, and cystic patterns. The cells showed voluminous eosinophilic cytoplasm with cytoplasmic basophilic granular stippling, characteristic of this tumor entity. Occasional intracytoplasmic globules were also noticed. The neoplastic cells had round nuclei with prominent, eosinophilic nucleoli, equivalent to ISUP (grade 2). Foci of clear cell cytoplasmic changes were also noticed as well as scattered collections of histiocytes. No features of high-grade transformation such as sarcomatoid or rhabdoid changes were identified (Figure 2).

Ancillary immunohistochemical studies were requested and showed strong positivity with AMACR, Vimentin, CD10 and faint nuclear staining for PAX8 (confirming renal origin). The neoplastic cells showed focal positivity of CK20, AE1/AE3 and CAM 5.2. It is completely negative for HMB45, Melan-A, CD117 and CK7 (Figure 3).

Based on the morphological and immunohistochemical findings, the diagnosis of Eosinophilic Solid and Cystic Renal Cell Carcinoma

(ESC-RCC) was rendered. Tissue was sent for chromosomal microarray study which revealed a loss of chromosome 9q34 (including TSC1 gene) and whole gains of chromosomes 7, 12 and 16p13 (including TSC2). The described abnormal genetic results were further confirmed using next generation sequencing study. This finding confirmed the diagnosis of ESC-RCC.

Follow-up computed tomography scan study (CT scan) of the chest, abdomen and pelvis was performed after one year of the surgery. It showed no evidence of local recurrence or distant metastasis.

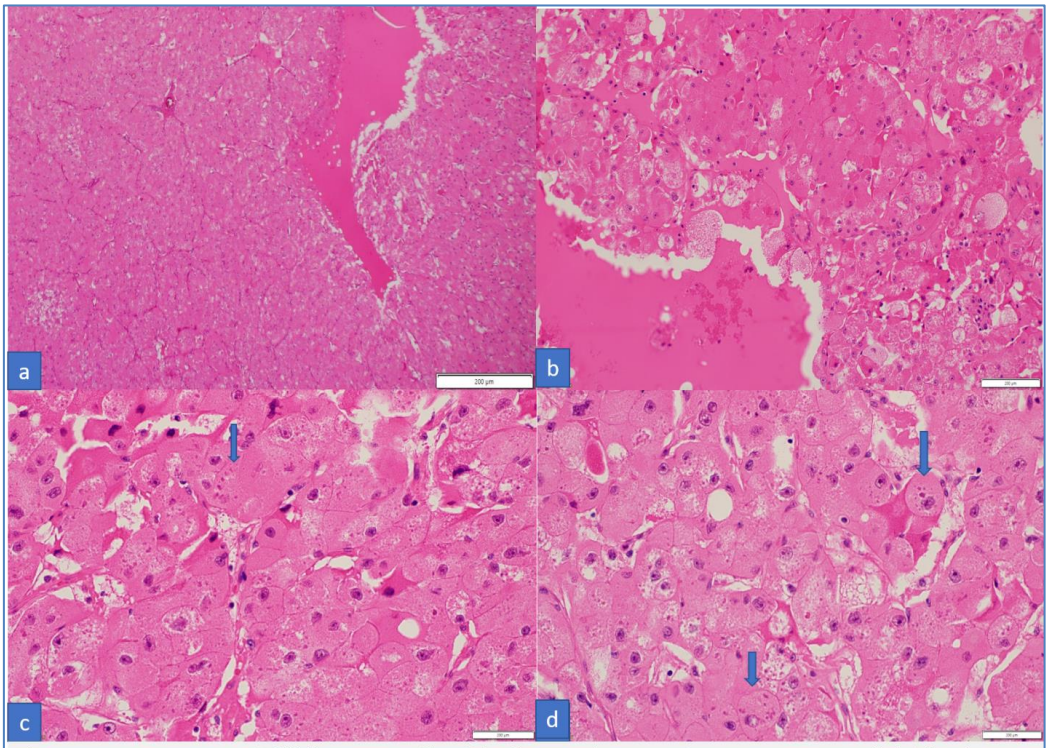

Figure 2. Microscopic pictures: (a&b) showing a variable solid and cystic architecture, H&E 100x, 200x respectively. (c&d) Higher magnification showing the characteristic basophilic cytoplasmic globules 'marked with an arrow', H&E 400x.

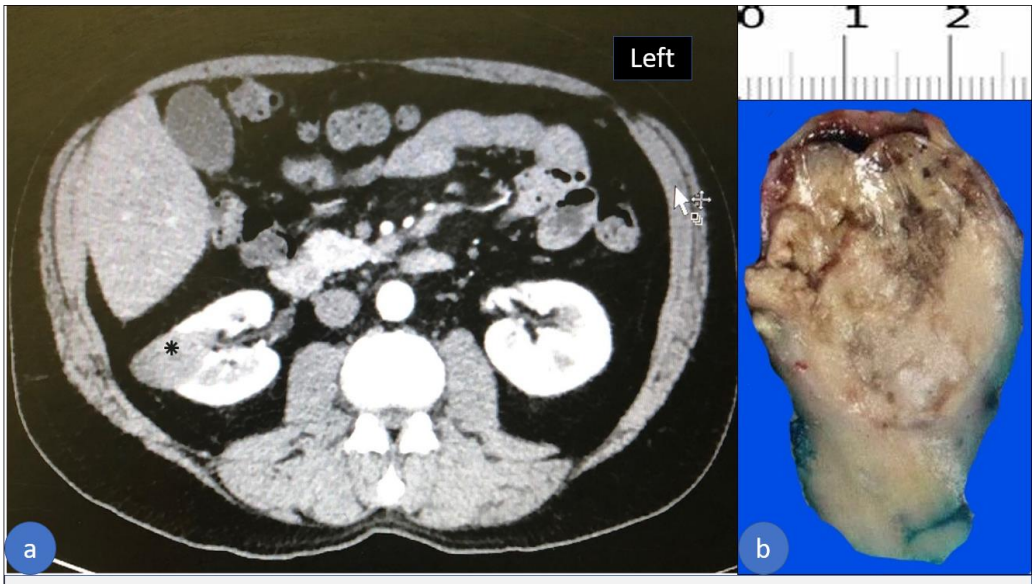

Figure 1. (a) CT scan, post contrast, with renal mass protocol showing a right kidney mass (marked with an asterisk), located in the lower pole of the right kidney. (b) Gross picture of the resected mass and part of the kidney, showing a variable solid and cystic cut surface.

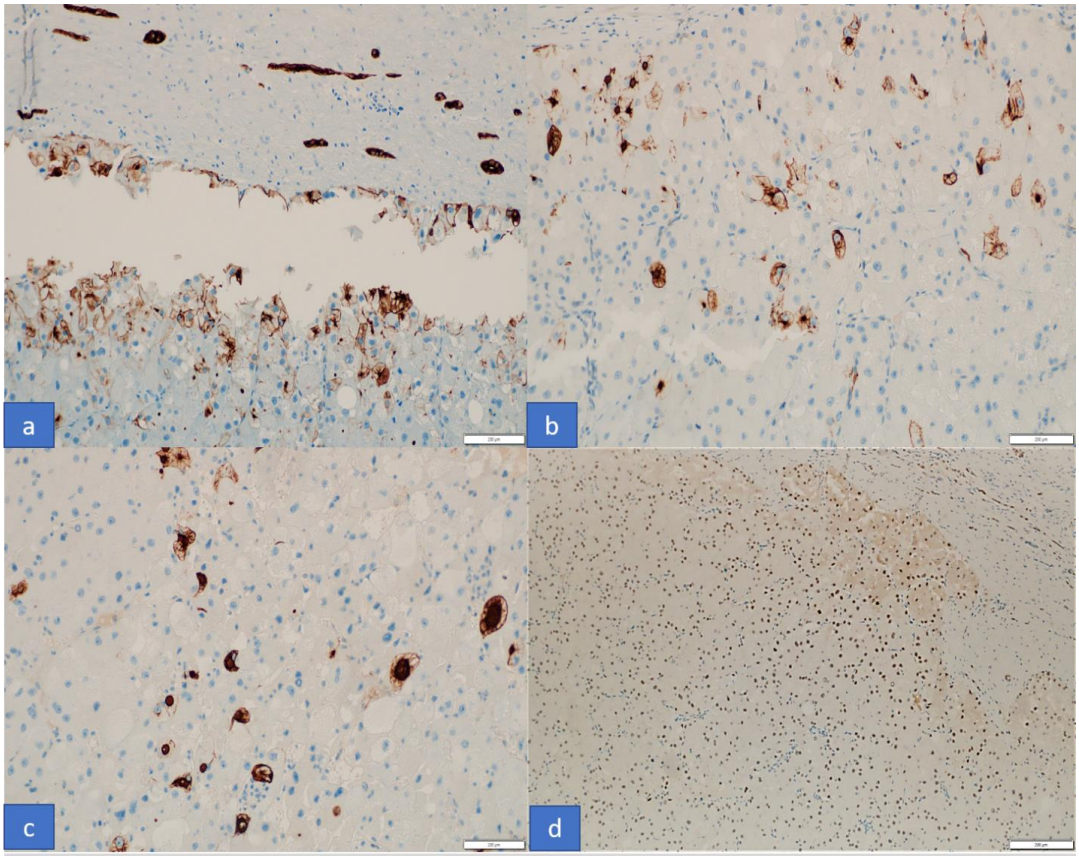

Figure 3. Focal immunoreactivity with Cam 5.2 (a) and CK20 (b&c) (200x). Nuclear staining with PAX8 (d) (200x)

DISCUSSION

Eosinophilic Solid and Cystic Renal Cell Carcinoma (ESC-RCC) was first described by Trpkov *et al.*, as a novel entity of renal neoplasms with characteristic clinical, pathological and molecular features. Grossly, ESC-RCC typically is a well circumscribed tumor which is tan in color, with variable consistency of areas exhibiting solid growth mixed with cystic spaces. The average greatest dimension is 50 mm. Many of the reported cases lack well-defined capsule, however, tumor encapsulation has been described [7], a feature that is present in our case.

Typically, the neoplastic cells are arranged in compact sheets with cystic spaces in between that are lined by cells with voluminous eosinophilic cytoplasm exhibiting hobnail arrangement. The cells exhibit abundant, deeply eosinophilic cytoplasm with characteristic basophilic granular stippling which signifies aggregates of endoplasmic reticulum on electron microscopy, a feature that was recognizable in many reported cases. The neoplastic cells exhibit foci of clear cell change as demonstrated in our case [4]. The consistent immunohistochemical finding in all reported cases is variable expression of CK20, with great majority of the cases show diffuse staining. Cases with patchy focal expression were also reported, as our case [1, 3]. Thirty cases showed focal expression of CK7 (4). None of the cases were negative for CK20 and positive for CK7. This finding warrants considering other neoplastic entities [6]. The neoplastic cells are classically positive for PAX8, Vimentin, CD10 (diffuse or focal) and AMACR while negative for CD117. CK8/18 and Pan-cytokeratin are expressed in 95%, and 100% of the cases reported, respectively [4].

The Differential diagnosis includes eosinophilic variant of clear cell RCC, oncocytic variant of chromophobe renal cell carcinoma, oncocytoma, epithelioid angiomyolipoma, and MiTF/TFE family translocation renal cell carcinoma, which typically show prominent vasculature combined with complete negativity of CK20. Oncocytic variant of chromophobe renal cell carcinoma is ruled out by the complete negativity for CD117 along with vimentin positivity and absence of nuclear irregularity or perinuclear clearing. Negativity for CD117 along with positivity for vimentin also excluded oncocytoma from the differential diagnosis [10].

Epithelioid angiomyolipoma is considered one of the strong differential diagnoses, given that it typically shows features of eosinophilic solid and cystic renal cell carcinoma including solid architecture with frequent intracytoplasmic vacuolization and focal clear cell changes [7]. The main cytological overlap is the cellular cytoplasmic similarity, as both entities are known to exhibit cells with voluminous eosinophilic

cytoplasm and prominent granularity. In general, nuclear pleomorphism is more significant in epithelioid angiomyolipoma than ESC RCCs [11]. In addition, Tretiakova MS. documented immuno-phenotypical similarity, as both tumours show expression of Melan-A and vimentin along with negativity of EMA, Pan-CK, CK7 and CD117 [7]. The application of PAX 8 immunohistochemical stain is useful, given that it is totally negative in epithelioid angiomyolipoma [12].

MiTF/TFE family translocation carcinoma needs to be considered in the list of differential diagnosis, given the similarities in morphological appearance, particularly in the subtype with TFEB gene abnormality. This possibility was excluded based on negative FISH study for TFEB gene rearrangement.

ESC- RCC is not yet designated as a separate entity in the World Health Organization 2016 classification of renal cell carcinoma [3-5]. Many of the cases were misclassified previously as "Renal Cell Carcinoma-Unclassified', thus, the true incidence of this tumor is still unknown [6]. To date, approximately 60 cases of this entity are reported. This neoplasm was thought to be almost exclusively found in adult female patients, however, cases in males are summarized in table 1 [1,2 ,7,8].

Generally, ESC-RCC is considered an indolent renal neoplasm [3, 4]. However, four reported cases have shown metastasis. Considering this fact, it is justified to use the term RCC to ensure clinical surveillance and close follow up of patients with this neoplasm [2, 6, 7, 9].

Although ECC-RCC has been documented in 10 % of tuberous sclerosis patients, the majority are sporadic with no relation to the TSC [13, 3, 4].

By reviewing the recent molecular studies of ESC-RCC, somatic, biallelic loss or mutation of TSC genes (either TSC1 or TSC2), has been documented to be strongly related to this neoplasm in phenotypically normal individuals. This finding could expand the potential therapeutic choices [10, 14].

CONCLUSION

Considering oncocytic renal neoplasms, Eosinophilic Solid and Cystic Renal Cell Carcinoma is a unique entity that is mainly affecting adult female patients with few reported cases in male patients. After reviewing medical English literature, this is the first reported case of ESC-RCC in elderly male patient that shows typical morphological and molecular alterations of ESC-RCC with only focal expression of CK 20.

Table-1: ESC-RCC Reports in Male Patients

Name of the first author/Case #	Age	Size/Stage
Li Y *et al*./Case 1	15	Multifocal (3.8 and 1.2 cm)/ pT1Nx
Li Y *et al*./Case 2	25	5 cm / pT1Nx
Li Y *et al*./Case 3	35	1.3 cm/ pT1Nx
Li Y *et al*./Case 4	34	cm / pT1Nx
Tretiakova MS./Case5	50	20.5 cm/ unknown
Chen YB *et al*. / Case 6	40	2.5 cm/ pT1a
Chen YB *et al*. / Case 7	59	3.6 cm/ pT1a
Chen YB *et al*./ Case 8	52	1.5cm/ pT1a

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