A case of a novel entity: eosinophilic solid and cystic renal cell carcinoma

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Abstract

Eosinophilic solid and cystic renal cell carcinoma (ESC-RCC) is a relatively newly described entity characterized by specific morphological features and a consistent immunohistochemical profile. The vast majority of cases are sporadic, but tumours with identical histological appearances have been reported in patients with tuberous sclerosis complex (TSC). The distinction between a sporadic or syndrome associated ESC-RCC is not possible without, at a minimum, exploring the patient's clinical context and family history. We present a case of a young female patient who presented with bilateral renal tumours, one of which has been diagnosed as ESC-RCC, and is awaiting genetic testing to exclude underlying TSC.

Keywords eosinophilic tumour; renal cell carcinoma; tuberous sclerosis

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Case report

A female patient in her late twenties presented to her GP with left sided abdominal pain. Splenomegaly was noted on clinical examination and subsequent ultrasound of her abdomen revealed bilateral renal tumours with different characteristics. Further imaging (CT abdomen) confirmed a well-defined, 15 cm left renal mass with cystic and solid components, and a smaller, 4 cm solid lesion in the right kidney. There were no other remarkable findings. The patient underwent an urgent radical left nephrectomy with plans to biopsy the right renal lesion at a later date.

Macroscopic assessment revealed a well-circumscribed, solid, and cystic tumour within the upper pole of the left kidney. There was no definite evidence of renal vein invasion or infiltration of hilar or perinephric fat.

Histological examination revealed a tumour composed of multiple cystic spaces of varying sizes interspersed with solid areas (Figure 1). The tumour cells were predominantly arranged in small clusters and nests with intervening delicate fibrous tissue. The cells were epithelioid with amphophilic to eosinophilic cytoplasm, round to oval nuclei and occasional visible nucleoli seen. In other areas, the cells appeared to have slightly granular, amphophilic material present within the cytoplasm. There was no evidence of lymphovascular invasion or other high grade features.

On immunohistochemistry (IHC), the tumour cells were positive for PAX-8, CK20, RCC marker, vimentin, AMACR and CD10. The cells were negative for CK7, CD117, BerEP4, S-100, Melan-A and HMB45. Figure 2 illustrates the pertinent IHC markers.

Based on these morphological features and supporting IHC, a provisional diagnosis of eosinophilic solid and cystic renal cell carcinoma (ESC-RCC) was made. Nonetheless, similar renal carcinomas can be seen in patients with tuberous sclerosis complex (TSC), therefore this syndrome must be excluded to determine if it is sporadic ESC-RCC or a TSC- associated RCC. Whilst the patient discussed in this case report does not have any stigmata of TSC and no family history of cancers, she has been referred for genetic testing, and awaits a biopsy of the contralateral right renal mass.

Discussion

ESC-RCCs are a novel subtype of renal neoplasms exhibiting distinct morphological, immunohistochemical and molecular features. They have a striking female predominance and are seen across a wide age range distribution, including paediatric patients.[1] These lesions typically show indolent behaviour, although rare cases of metastasis to lymph nodes, liver, lung, and bone have been reported.[1,2] The true incidence is difficult to determine as this entity would have previously been categorized as "unclassified (eosinophilic) carcinomas".[1]

Grossly, ESC-RCC tumours are well-circumscribed with solid areas and variably sized cysts.[2] On histology, the tumour cells within the solid areas show either diffuse, acinar or nested growth patterns.[1] The cystic spaces can be admixed with the solid foci and are typically lined by neoplastic cells with voluminous eosinophilic cytoplasm, commonly with a hobnail appearance.[2] The neoplastic cells typically show eosinophilic, abundant cytoplasm with round to oval nuclei, and very occasional prominent nucleoli.[1,2] The most characteristic feature is coarse cytoplasmic granules, commonly referred to as 'stippling'.[1,2] Foci of foamy histiocytes and lymphocytes are sometimes found.[2]

ESC-RCC tumours have a distinct IHC profile. CK20 positivity (diffuse or focal) is present in approximately 85% of cases, alongside a negative CK7 stain.[1] Other positive stains include nuclear

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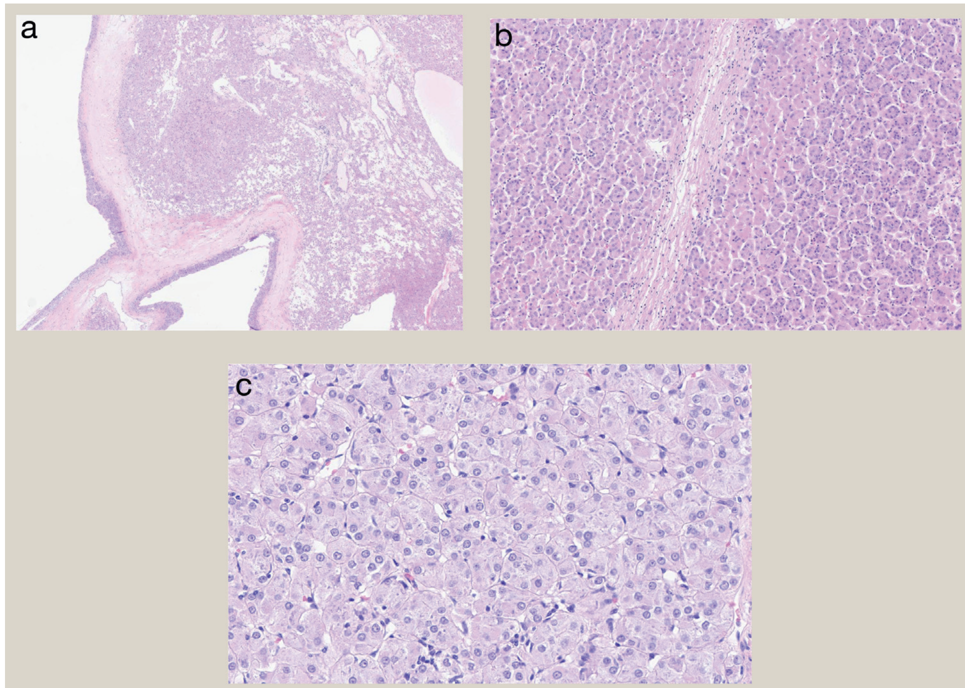

Figure 1 Morphological features of eosinophilic solid and cystic renal cell carcinoma. (**a**) Low power magnification showing solid and cystic areas. (**b**) Neoplastic epithelioid cells with voluminous cytoplasm arranged in nests with intervening fibrous tissue. (**c**) Slightly granular, amphophilic material seen within the cytoplasm of some cells.

PAX-8 expression, vimentin, AE1/3, CK8/18 and RCC marker.[1] There is typically no reactivity for CD117, CAIX and HMB45.[1]

Whilst ESC-RCC tumours are typically sporadic, there is a subset of histologically identical renal neoplasms reported in patients with tuberous sclerosis; an autosomal dominant multisystem disorder resulting from mutations in the TSC1 or TSC2 genes.[3] It is important to be aware of the patient's current and previous clinical presentations, and family history, as there

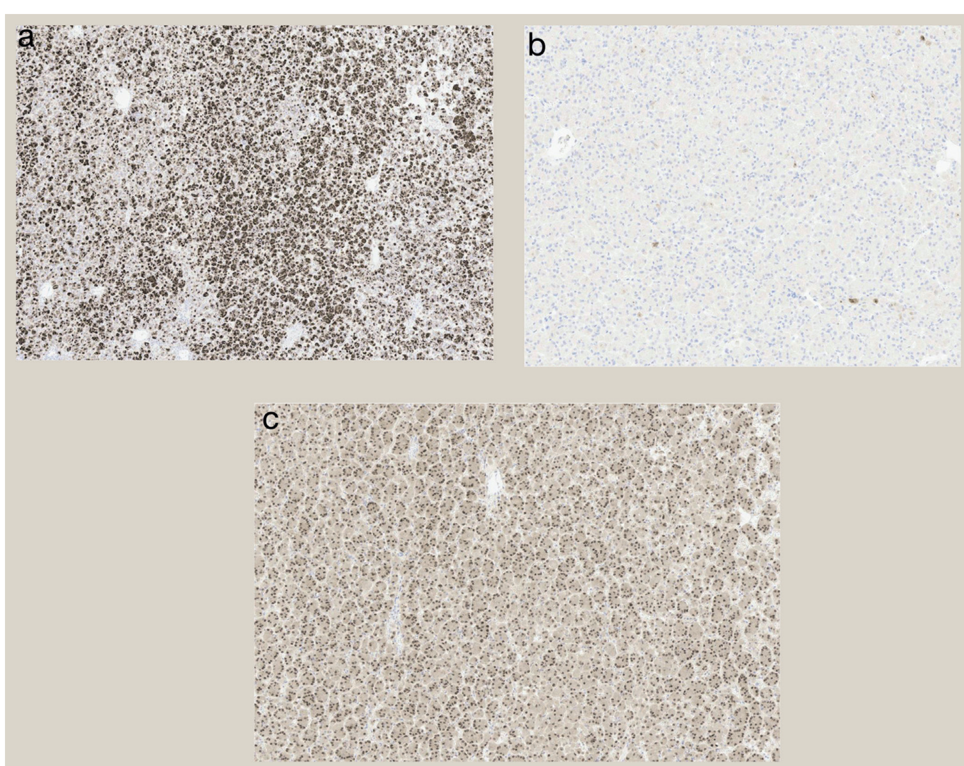

Figure 2 Typical immunohistochemical profiles. (**a**) Positive staining for CK20. (**b**) Negative staining for CK7. (**c**) Positive nuclear staining for PAX-8.

can be crucial clues to help distinguish between a sporadic or syndromic ESC-RCC. In general, TSC-associated RCCs are seen more frequently in younger patients, tend to be multifocal and/or bilateral and demonstrate greater morphological heterogeneity.[3]

Conclusion

ESC-RCC is a novel entity predominantly seen in female individuals with distinct morphological features and a consistent immunohistochemistry profile. These tumours exhibit indolent behaviour with rare cases of metastasis reported in the literature. Histologically, ESC-RCCs are indistinguishable from TSC-RCCs; therefore, recognition of this entity should prompt pathologists to investigate the clinical context and consider the possibility of underlying TSC. The patient in our case report has been referred for genetic testing, highlighting the fact that consideration of this important differential can influence subsequent management strategies, and impact outcomes for the patient. ◆

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Practice points

- ESC-RCC are indolent tumours seen across a wide age distribution and occur predominantly in female patients.
- Exercise caution when making a diagnosis of sporadic ESC-RCC — could this patient have underlying tuberous sclerosis?
- ESC-RCC tumours typically show the following IHC profile: CK20+/CK7-, PAX-8+, CD117-.

Self-assessment multiple choice questions

1. Which combination of immunohistochemistry markers are typical for ESC-RCC tumours?

a. CK20-, CK7+, PAX-8+, CD117-, vimentin−
b. CK20+, CK7+, PAX-8+, CD117 -, vimentin+
c. CK20+, CK7-, PAX-8+, CD117-, vimentin+
d. CK20+, CK7-, PAX-8+, CD117+, vimentin-
e. CK20+, CK7+, PAX-8-, CD117-, vimentin+

Answer: C

2. What is the characteristic feature seen on histology for ESC-RCC tumours?

a. Abundant basophilic cytoplasm
b. Coarse cytoplasmic granules
c. Nuclear grooves
d. Prominent eosinophilic nucleoli
e. Irregular nuclear outlines

Answer: B

3. Which of the following statements is correct?

a. Tuberous sclerosis complex (TSC) has an autosomal recessive inheritance pattern.
b. TSC-associated RCCs tend to be more aggressive.
c. TSC-associated RCCS are typically seen in older individuals.
d. TSC-associated RCCs tend to be multifocal and/or bilateral.

Answer: D