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CASE STUDY

Eosinophilic solid and cystic renal cell carcinoma – an emerging renal tumour with a good prognosis

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Eosinophilic solid and cystic renal cell carcinoma is an uncommon, recently recognised, malignant renal tumour that has distinctive pathological and genetic features. This tumour enters into the histological differential diagnosis of a renal tumour with eosinophilic cytoplasm. It is important to recognise because it has a generally favourable prognosis and may prompt genetic testing due to its association with mutations in the tuberous sclerosis complex genes. We present two cases of renal carcinoma, occurring in a 19-year-old man and a 42-year-old woman, both discovered incidentally, showing similar pathological features and having low stage disease. The purpose of this report is to increase awareness of this uncommon renal tumour, to aid in its recognition by pathologists and to alert treating clinicians to its typically indolent behaviour and genetic associations.

Keywords: renal cell carcinoma, eosinophilic solid and cystic renal cell carcinoma, tuberous sclerosis complex, immunohistochemistry, renal tumour

Introduction

Renal cell carcinoma (RCC) is recognised as one of the most common cancers worldwide. Advances over the past few decades have brought about recognition of an increasing number of new renal cancer entities, many of which are not formally classified in the 2016 World Health Organization (WHO) classification of renal tumours. Eosinophilic solid and cystic renal cell carcinoma (ESC RCC) is one of these newly recognised entities which has a generally more favourable prognosis and important genetic associations. We present two recent cases seen at our institutions, to highlight the most important diagnostic features and the clinical importance of recognising this uncommon emerging renal tumour.

Case report: case 1

A 42-year-old woman presented incidentally while being worked up as a live renal donor. She had no previous medical history and was asymptomatic at the time of diagnosis. She was found to have a left renal mid-pole cystic lesion, measuring 26 x 25 x 24 mm, on routine ultrasound. The lesion was classified on computed tomography (CT) scan as a Bosniak III cyst (Figure 1). Laparoscopic partial nephrectomy was performed and the patient made an uneventful recovery. The patient was followed up according to the standard RCC protocol at four months post-surgery with a repeat CT scan, which showed no evidence of disease recurrence or new disease.

The cystic lesion was submitted for pathological examination. It was opened surgically along the longitudinal axis and had no visible contents. The cyst wall fragments were yellow-white in appearance.

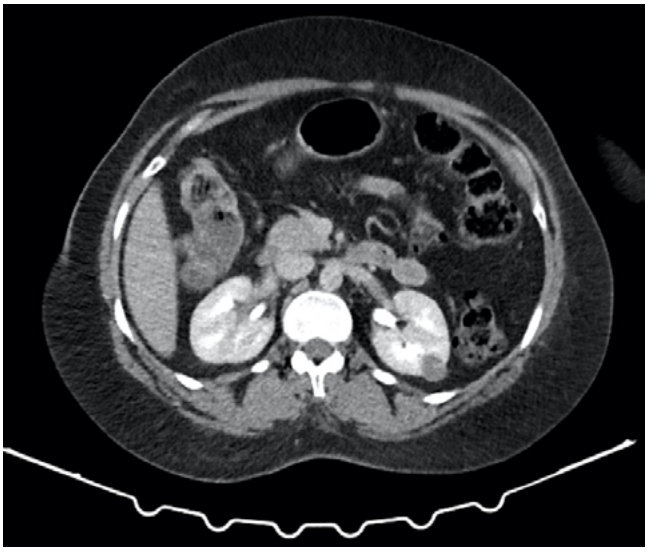

Figure 1: Axial view of the contrasted CT scan shows a left mid-pole cortical renal cyst with slight heterogenous attenuation (Bosniak III cyst)

Histological sections showed a solid and cystic neoplasm comprising deeply eosinophilic epithelial cells in a focally solid and otherwise macrocystic configuration (Figure 2). The neoplastic cells had round nuclei with variably prominent nucleoli and focal multinucleation, as well as a vague granular quality to the cytoplasm. Frequent basophilic intracytoplasmic inclusions were noted (Figure 3). The cystic spaces were lined by a similar population of eosinophilic cells that exhibited a hobnail appearance. Scattered aggregates of foamy macrophages were seen throughout, as well as moderately dense background lymphocytic inflammation and prominent vascularity. The immunohistochemical staining profile was as follows: CK20,

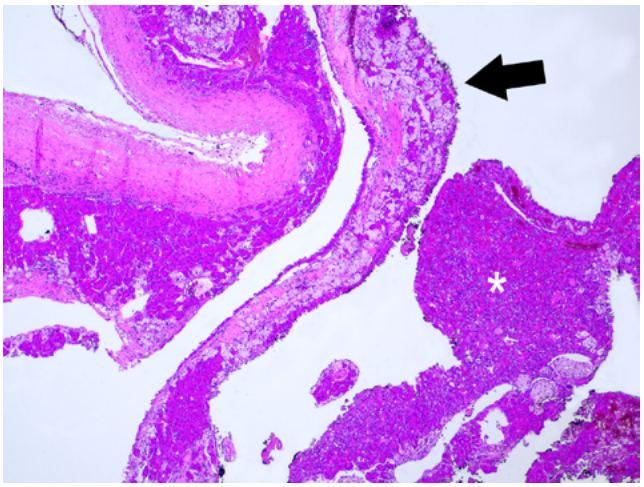

Figure 2: The variable solid (asterisk) and cystic (arrow) architecture of the renal tumour is highlighted at low magnification (haematoxylin & eosin, 100x)

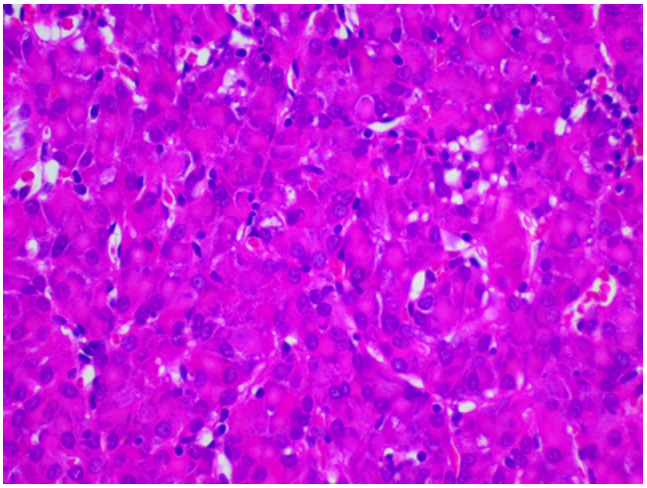

Figure 3: High magnification reveals eosinophilic tumour cells with basophilic intracytoplasmic inclusions (haematoxylin & eosin, 400x)

PAX8, vimentin and CD10 positive in the neoplastic cells; CK7, CD117 and P504S negative.

Case report: case 2

A 19-year-old man presented to casualty with sudden onset atypical chest pain. He had no prior medical history. Owing to some Marfanoid features, a contrasted CT scan was performed to exclude aortic dissection. The presence of an incidental left renal mass was noted on imaging. This was a large mixed solid and cystic tumour arising from the upper pole and measuring 50 x 43 x 38 mm (Figure 4). Both kidneys were incompletely rotated and showed multiple accessory arteries bilaterally. There were no abnormalities found to account for the chest pain and it resolved spontaneously. His preoperative renal function tests were normal. A laparoscopic nephrectomy was performed. Postoperative recovery was uneventful.

Gross examination revealed a partly necrotic solid and cystic encapsulated mass arising in the upper pole of the kidney (Figure 5). The tumour was limited to the renal parenchyma with no involvement of perinephric fat or the renal sinus. Histology showed a RCC with solid and cystic growth comprising large epithelial cells

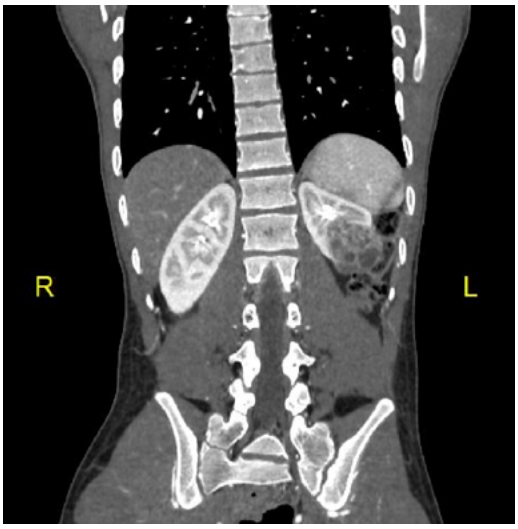

Figure 4: Coronal view of the contrasted CT shows a solid and cystic tumour arising in the upper pole of the malrotated left kidney

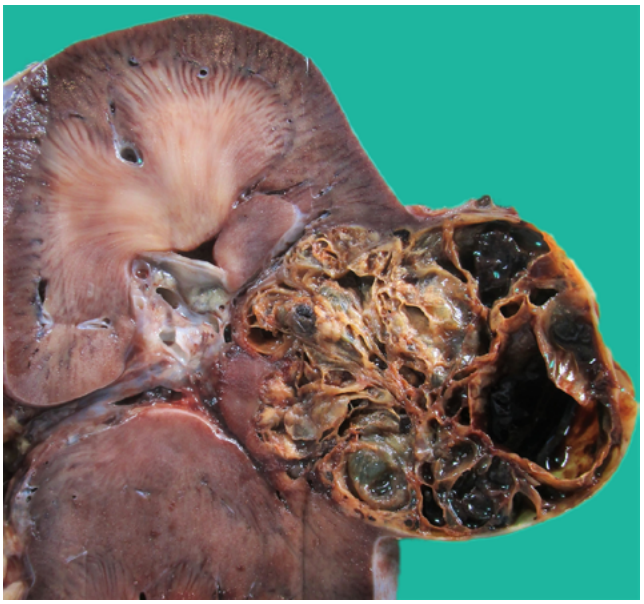

Figure 5: Cut section of the kidney revealed a solid and cystic septate tumour with areas of haemorrhage and pale nodules

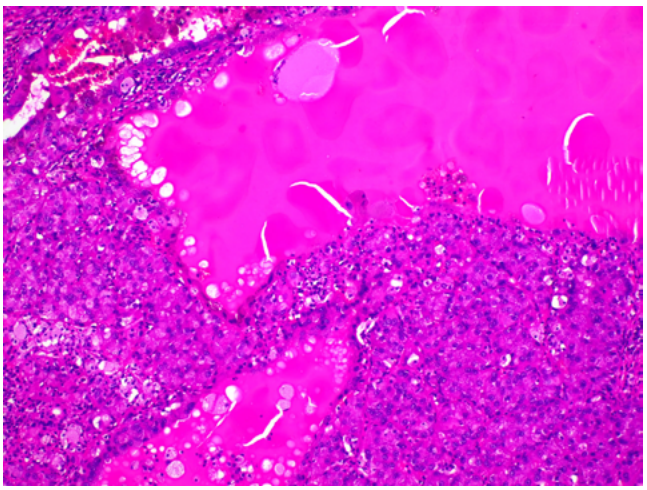

Figure 6: Low magnification demonstrates microcystic, solid and nested growth comprising cells with voluminous eosinophilic cytoplasm, evidence of prior haemorrhage and focal dystrophic calcification (haematoxylin & eosin, 100x)

with abundant eosinophilic cytoplasm. Papillary, pseudopapillary, solid and glandular elements were demonstrated (Figure 6). The tumoural cells contained large round nuclei with single small discrete nucleoli and coarse chromatin. Areas of necrosis and prior haemorrhage were present. Basophilic cytoplasmic inclusions were noted in areas. This tumour showed positive immunolabelling with PAX8, CK20 and CD10. CK7, EMA, carbonic anhydrase 9, CD117, Melan A and TFE3 were negative.

Discussion

RCC is the fourteenth leading cause of cancer worldwide, with 431 288 new cases reported in 2020 by the WHO Global Cancer Observatory, and a lifetime risk of 1.7% according to SEER data.[1,2] Over the past two decades, there has been a dramatic increase in the number of histologically recognised RCC variants. These are important to be aware of and recognise as they have different implications for the patient in terms of prognosis, and may have genetic associations. ESC RCC is one of these recently described entities which has characteristic histology and a generally favourable prognosis.[3] This entity was initially described in 2010 by Schreiner et al. and is now increasingly recognised.[4,5] ESC RCC will be included as a histological subtype of RCC in the upcoming 5th iteration of the WHO classification of renal tumours.[6] Its recognition is of clinical importance as it generally has a good prognosis, presents at a low clinical stage and has implications for genetic testing.[7]

Many of the initial case reports of ESC RCC were found to be associated with tuberous sclerosis complex (TSC) in patients harbouring germline TSC mutations, but it has been recently demonstrated that most cases are sporadic, harbouring somatic TSC1 and TSC2 mutations. The syndromic cases are now estimated to represent a minority of approximately 10% of cases.[8] Neither of the cases presented in our series had clinical manifestations of TSC. Further molecular karyotyping of ESC RCC has shown recurring genomic alterations including copy number (CN) gains at 16p13-16q23, 7p21-7q36, 13q14 and 19p12, CN losses at Xp11.21 and 22q11 and loss of heterozygosity (LOH) alterations at 16p11.2-11.1, Xq11-13, Xq13-21, 11p11, 9q21-22 and 9q33.[9] These alterations are unique to ESC RCC and provide additional genetic evidence that this tumour should be regarded as a distinct entity.[9] The age range at initial presentation is wide (32–79 years) with an overall female predominance.[7,9,10] In most cases, these tumours behave in an indolent fashion with only exceptional cases showing an aggressive clinical course and associated metastatic disease.[11]

The histological features of ESC RCC are characteristic and include variably solid, macro- and microcystic architecture with or without papillary projections. These tumours are generally well circumscribed and are composed of large epithelial cells with voluminous eosinophilic cytoplasm commonly showing basophilic granular cytoplasmic inclusions ('stippling'). These inclusions have been identified on electron microscopy as intracytoplasmic aggregates of rough endoplasmic reticulum.[3,7,9,10] Other common features include aggregates of foamy macrophages, lymphocytes and increased vascularity in the background. Immunohistochemistry for these tumours is characteristic, with a unique CK20-positive/CK7-negative profile.

There is a broad histological differential diagnosis for RCCs with eosinophilic cytoplasm including oncocytoma, chromophobe RCC, epithelioid angiomyolipoma, hybrid oncocytic tumour, tubulocystic carcinoma, papillary RCC, microphthalmia-associated transcription (MiT) family translocation RCC, clear cell (conventional) renal cell carcinoma with eosinophilic cytoplasm, ALK translocation RCC, SDH deficient RCC, and metastases (especially from adrenal and liver primaries).[12] This differential includes benign and malignant tumours which often have overlapping preoperative clinical features. Judicious use of immunohistochemistry, supplemented where necessary with molecular testing will help to distinguish these tumours. ESC RCC is the only renal tumour that shows CK20 positivity. Awareness of this should prompt the pathologist to add CK20 to the panel of immunohistochemical stains when presented with a solid and cystic renal tumour composed of large eosinophilic cells.

Conclusion

In conclusion, the importance of this entity should be highlighted as a new and emerging distinct renal tumour, as increased awareness will enable more ready diagnosis by pathologists. The clinical implications for prognostication and postoperative treatment approaches are significant for treating clinicians and have been highlighted above. Furthermore, additional studies are required to better understand the epidemiology, pathogenesis and prognosis of these uncommon tumours.

Conflict of interest

The authors declare no conflicts of interest.

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