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Case Series

Interesting malignant renal tumours: a tripod of cases

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ABSTRACT

Renal malignancy is the 15th leading cause of annual deaths, with late detection and misdiagnosis leading to decreased patient survival. We hereby present three cases of malignant renal tumours which grabbed our attention because of their rarity and interesting presentation. Case 1-A 38 year old male presented with palpable lump in right flank, CT revealed a multilocular cystic lesion in right kidney, along with horse-shoe kidneys. In view of renal biopsy suggesting Tubulocystic carcinoma, patient underwent nephrectomy and diagnosis confirmed to be the same histomorphologically as well as immunohistochemically using AMACR and PR. Case 2-A 77-year-old male had lower urinary tract symptoms due to prostatomegaly, and a left renal mass and small hepatic cysts were detected incidentally. Kidney function was normal. Microscopy showed Chromophobe renal cell carcinoma, which was confirmed with immunohistochemical markers CK7 and CKIT. Case 3-A 50 year female presented with recurrent lump in her left flank, CT confirmed a huge left renal fossa mass. Biopsy showed features of malignant mesenchymal neoplasm consistent with leiomyosarcoma based on immunohistochemical panel of vimentin, h-Caldesmon, SMA, EMA, HMB-45 and S100, which helped in differentiating it from tumours like angiomyolipoma. Renal tumours have varied morphological overlapping and it is important to rule out close differentials using immunohistochemistry before coming to a diagnosis. Awareness of such presentations and findings can broaden our understanding of renal tumours which can help in early and accurate diagnosis for better outcome of the patient.

Keywords: Renal tumours, Kidney neoplasms, Renal cell carcinoma, Tubulocystic renal cell carcinoma, Chromophobe, Leiomyosarcoma

INTRODUCTION

Renal malignancy has been reported by GLOBOCAN 2020 to be the 14th leading cause of new cases and 15th leading cause of deaths worldwide. In India, the numbers are relatively less, with an incidence of 16,861 in 2020, making it the 21st common cause of new cases, and the 22nd leading cause of mortality in the same year.[1] This is due to many undiagnosed and underreported cases in the Indian population mainly because of the incidental presentation and diagnostic difficulties.

The current classification of renal tumours in the 2022 WHO blue book is much detailed. However, owing to a handful of entities dominating the spectrum, there are less incidence reports and discussions about the not so common renal malignancies, leading to misdiagnosis because of mimicking features.

Tubulocystic renal cell carcinoma (TCRCC) is a rare distinct subtype of renal cell carcinoma accounting for less than 1% of renal tumours.[2] It is mostly an incidental finding with a predilection for males. TCRCC is a great imitator, and can be confused with benign cystic lesions or aggressive renal malignancies.[3] It is usually indolent, but there are rare reports of recurrence or metastasis.[4]

Chromophobe renal cell carcinoma (ChRCC), although not rare, accounts for only 5-7% of renal neoplasms. Most patients have an asymptomatic presentation, and some are associated with hereditary syndromes like Birt-Hogg-Dubé syndrome. ChRCC is considered to have favourable

clinical course compared to the more common renal malignancies. However, a small proportion of patients develop recurrence or metastasis in 6-7% cases, most commonly in liver (39%) and lung (36%).[5]

Primary renal leiomyosarcoma is a rare and aggressive mesenchymal tumour, representing about 1-2% of all renal malignancies. It arises from the smooth muscle cells of intrarenal blood vessels, renal capsule or renal pelvis and has a high propensity for local recurrence and distant metastasis, hence complete surgical resection is a must. Since it is a rare malignancy, diagnosis should be made with caution due to more common close differentials.[6]

Hereby report these 3 cases of malignant renal tumours which grabbed our attention because of their rarity and features similar to more common renal tumours.

CASE SERIES

Case 1

A 38 year old male presented to the urology OPD of IGIMS Patna with a history of abdominal fullness and intermittent right flank pain, with no urinary symptoms. Clinically, a non-tender lump was palpable in the right flank. Blood and urine tests found no abnormalities.

CT urography and CECT abdomen revealed horse-shoe kidneys, large multilocular cystic lesion in mid, upper pole of right kidney (Figure 1 A). Renal doppler showed no evidence of thrombosis in renal vein and IVC. DTPA scan showed reduced relative functioning of right kidney.

USG guided renal biopsy was done initially, and we grossly received multiple fragmented linear cores, ranging from 0.1 to 0.5 cm. Microscopically, variable sized tubules and cysts were seen separated by fibrous septa, and lined by cuboidal epithelium comprising tumour cells, some showing hobnailing pattern (Figure 1 B and C). Tumour cells had abundant eosinophilic cytoplasm, and enlarged nuclei with prominent nucleoli at 10× magnification, having WHO/ international society of urological pathology (WHO/ISUP) grade 3. Immunostaining revealed that tumour was cytoplasmic positive with AMACR and negative for PR, thus helping us make a diagnosis of TCRCC (Figure 1 D and E).

The patient underwent radical nephrectomy and we received a gross specimen of right kidney measuring 13×11×10 cm which had a bosselated external surface. Cut surface showed a grey white well circumscribed tumour measuring 12×9×8 cm covering almost the entire kidney and leading to loss of corticomedullary differentiation. The tumour had small cystic spaces rendering a bubble-wrap appearance (Figure 2 A and B).

Microscopically, the findings correlated with that of USG guided renal biopsy, and all sections showed variable sized tubules and cysts lined by cuboidal epithelium with areas of hobnailing, tumour cells having WHO/ISUP Grade 3 nuclei with minimal mitotic activity and atypia, and patchy necrosis (Figure 2 C and D). There was no lymphovascular invasion or perineural invasion. Renal sinus, renal vessels and ureter were unremarkable. The tumour cells were strongly positive for AMACR and negative for PR, which led to confirmation of our final diagnosis of TCRCC (Figure 2 E and F).

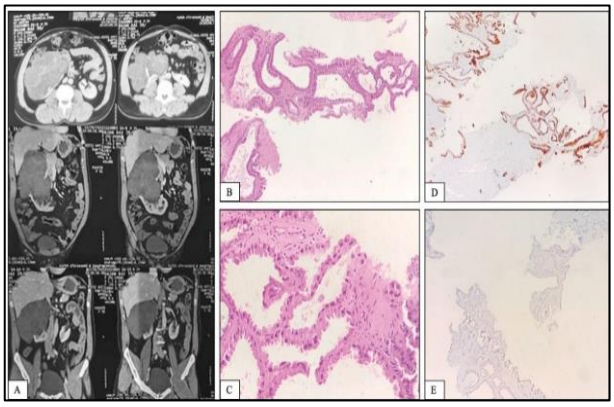

Figure 1 (A-E): Case 1 with radiographic and microscopic findings of USG guided renal biopsy. CECT abdomen of a large mass in right kidney. Renal tumour with variable sized tubules and cysts separated by fibrous septa, H and E-stained section, 10x magnification. Cuboidal epithelial lining of tubules and cysts with hobnailing pattern, enlarged nuclei and prominent nucleoli, H and E stain, 40x magnification. Immunohistochemistry showing AMACR cytoplasmic positivity, 10x magnification. Immunohistochemistry of PR negativity, 10x magnification.

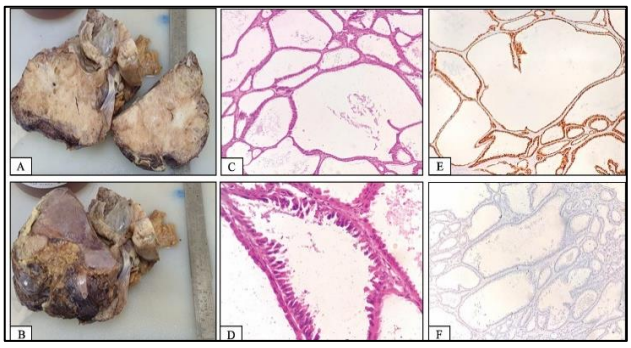

Figure 2 (A-F): Case 1 with right radical nephrectomy gross, histomorphological and immunohistochemical findings. Gross specimen of right kidney with a tumour covering entire kidney and having a bubble-wrap appearance. Entire tumour having tubulocystic appearance, H and E-stained section, 10x magnification. Tubules and cysts with lining tumour cells exhibiting classical hobnailing pattern, H and E stain, 40x magnification. Immunohistochemical demonstration of cytoplasmic AMACR positivity in tumour cells, 10x magnification. PR negative on immunohistochemistry, 10x magnification.

Case 2

A 77 year old male presented to the OPD with only lower urinary tract symptoms, but having no history of haematuria. No lump was clinically palpable. Blood investigations revealed Serum PSA level 13.4 ng/ml.

USG Whole Abdomen revealed prostatomegaly with a 51 gm prostate, incidentally detected few small hepatic cysts (Figure 3A and B), and a 4.8×3.6 cm mass in upper pole of left kidney. CT IVU was done which confirmed the left renal mass (Figure 3 C) and DTPA scan showed bilateral normally functioning kidneys.

The patient underwent radical nephrectomy, and we received a gross specimen of left kidney measuring 10×5×5 cm having a bosselated external surface. On sectioning, a unifocal well circumscribed unencapsulated grey brown tumour measuring 4.5×4×4 cm was noted at the upper pole, with focal areas of haemorrhage and no area of necrosis (Figure 3 D and E). Tumour was seen reaching upto the renal capsule, but perinephric fat and Gerota's fascia were free of tumour grossly. Ureteric and renal vessels resection margin were 5 cm away from the tumour.

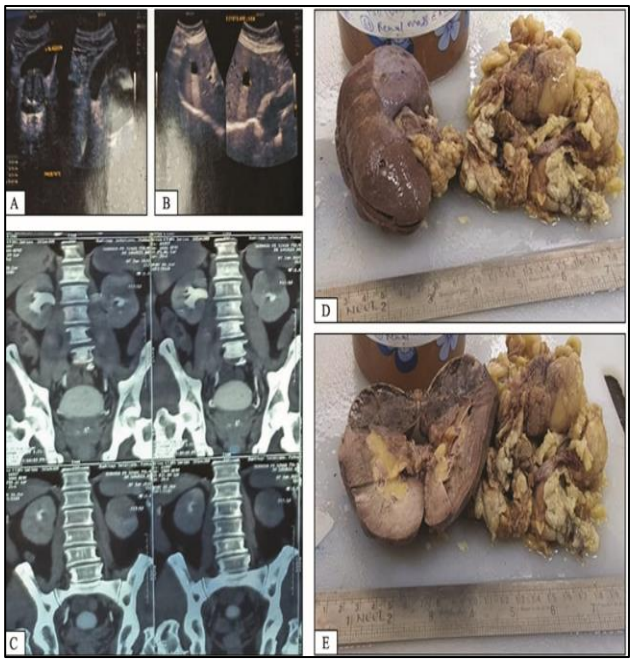

Figure 3 (A-E): Case 2 with incidentally detected mass in left kidney, radiographic and gross findings. Few small hepatic cysts on USG abdomen. CT IVU showing a mass in upper pole of left kidney. Gross specimen of left kidney with a well circumscribed grey brown tumour at the upper pole.

Microscopically, sections showed tumour cells arranged in sheets in a mosaic pattern with intervening thick fibrovascular septae (Figure 4 A). The tumour cells had prominent plant-like cell borders and abundant reticular cytoplasm. Nuclei of the cells were irregular, raisinoid with coarse chromatin and perinuclear halo (Figure 4 B). No areas of necrosis or sarcomatoid features were identified. There was no lymphovascular or perineural extension. Tumour was seen to extend upto renal capsule but not beyond it. Renal sinus, perinephric fat, Gerota's fascia, renal vessels and ureteric resection margin were all microscopically free of tumour. Immunohistochemistry showed the tumour to be diffusely cytoplasmic and membrane positive for CK7 and membrane positive for CD117 (Figure 4 C and D). This led to our final diagnosis of ChRCC, classic type.

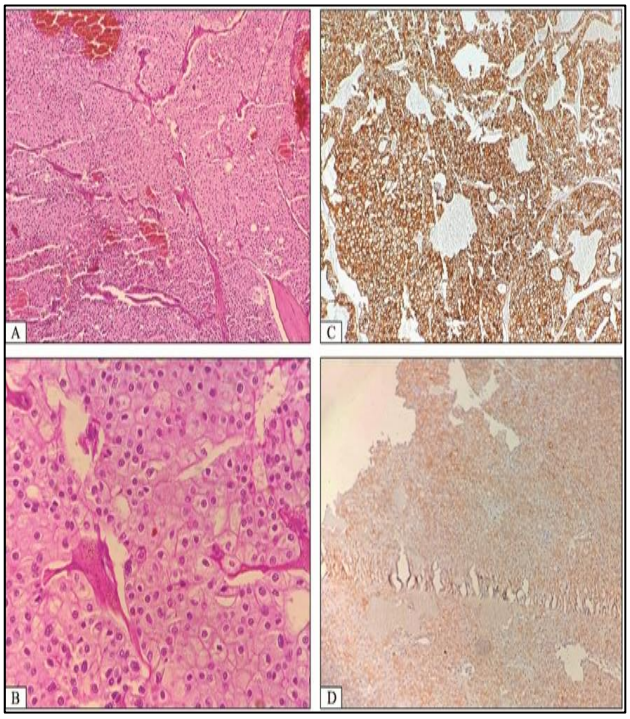

Figure 4 (A-D): Case 2 showing histomorphological and immunohistochemical features consistent with chromophobe renal cell carcinoma. Microscopy showing tumour cells arranged in sheets with thick fibrovascular septae, H and E stain, 10x magnification. Tumour cells having prominent cell borders, abundant reticular cytoplasm, irregular raisinoid nuclei and perinuclear halo, H and E stain, 40x magnification. Immunohistochemistry showing the tumour with diffuse cytoplasmic and membrane positivity for CK7, 10x magnification. Tumour cells membrane positive for immunohistochemical marker CD117, 10x magnification.

Case 3

A 50 year old female visited our urology OPD with a recurrent lump in her left flank region associated with dull aching pain and no history of haematuria. She had previously undergone partial nephrectomy for left renal mass at a peripheral hospital 2 years back, documents of which were unavailable. Clinical examination revealed a palpable non tender lump at her left flank. Blood and urine tests were normal.

USG Whole Abdomen was done which showed a hypoechoic mass in left renal fossa. CT Abdomen confirmed a left renal fossa mass measuring 20×14.8×14.3 cm and causing displacement of adjacent organs (Figure 5 A).

The patient underwent image guided renal biopsy, and we received 4 linear cores, ranging from 0.5 to 1 cm.

Microscopic examination of the sections from the left renal fossa mass showed fascicular growth pattern of the tumour cells with palisading (Figure 5 B). Individual tumour cells were atypical spindle to oval with eosinophilic fibrillary cytoplasm and blunt ended cigar shaped nuclei (Figure 5 C). There were 3-4 mitotic figures/10 HPF and small areas of necrosis. However, no area of adipocytes or proliferated blood vessels were seen. Immunohistochemistry showed tumour cells with diffuse strong positivity for h-Caldesmon and SMA, moderate Vimentin positivity, focal weak positivity for EMA, and S100 and HMB45 negative (Figure 6 A-F). This helped to rule out close differentials like renal epithelioid angiomyolipoma (EAML), and arrive at our final diagnosis of renal LMS.

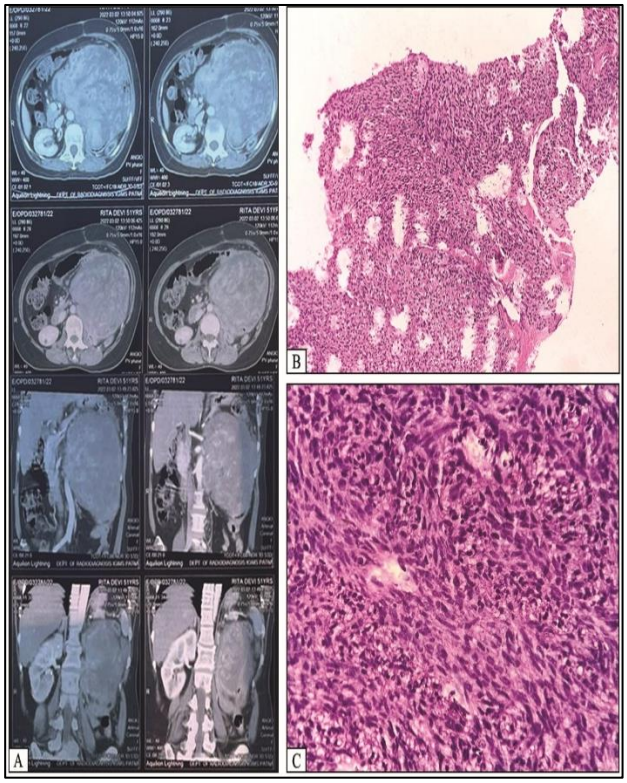

Figure 5 (A-C): Case 3 with a recurrent left renal mass, CT and microscopic findings. CT abdomen showing a huge left renal fossa mass causing displacement of adjacent organs. Microscopy showing fascicular growth pattern of the tumour cells, H and E section, 10x magnification. Atypical spindle to oval shaped tumour cells with eosinophilic fibrillary cytoplasm and blunt ended cigar shaped nuclei, H and E section, 40x magnification.

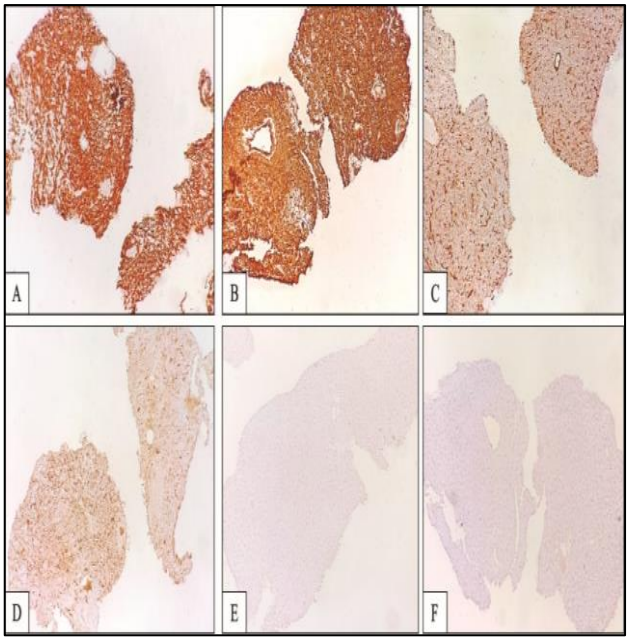

Figure 6 (A-F): Case 3 with immunohistochemical findings. h-Caldesmon shows tumour cells diffusely and strongly positive, 10x magnification. SMA showing tumour cells diffusely and strongly positive, 10x magnification. Vimentin showing moderate positivity in tumour cells, 10x magnification. EMA showing focal weak positivity, 10x magnification. S100 negative in tumour cells, 10x magnification. HMB45 negative in tumour cells, 10x magnification.

DISCUSSION

TCRCC is a rare subtype and presentation with horse shoe kidneys has not yet been reported. Incidence of horse-shoe kidneys in Indian population is 1 in 600-800 individuals. Currently, there are over 200 reports of tumours in the horse-shoe kidney. Balawender et al reported that renal cell carcinoma was the most commonly detected tumour, followed by Wilms tumour and transitional cell carcinoma.[7]

TCRCC has often been confused with other cystic lesions of the kidney like cystic nephroma (CN), mixed epithelial and stromal tumour (MEST) and multilocular cystic renal neoplasm of low malignant potential (MCNLMP). CN and MEST have a female predominance. CN is entirely cystic like TCRCC whereas MEST has a variable solid component. Hobnailing is present in both but they are infrequent as compared to TCRCC.[8] The intervening septa of CN is mostly thin and cellular, sometimes resembling ovarian stroma. On the other hand, MEST contains a broad stroma that is ovarian type. Because of this stromal component, both CN and MEST are immunohistochemically positive for PR.

MCNLMP contains cystic spaces lined by optically clear, bland looking cells with small nuclei of WHO/ISUP grade 1 or 2, and necrosis should be absent. Because of a

lack of these findings, MCNLMP was ruled out from our differentials.

TCRCC has also been often misdiagnosed as renal cyst, because of which only renal cyst marsupialization was done. Once a diagnosis of TCRCC is confirmed, nephrectomy is the standard treatment.

Majority of TCRCC are indolent, but those with de-differentiated foci can have metastasis and local recurrences in abdomen, pelvis and bones. A tumour morphologically favours TCRCC when the entire area examined shows variable sized tubules and cysts lined by tumour cells. On encountering areas of de-differentiation, the possibility of the more aggressive Fumarate hydratase (FH)-deficient renal cell carcinoma has to be eliminated. FH deficient renal cell carcinoma was ruled out from our differentials due to lack of such areas, and absence of prominent inclusion like nucleoli with perinucleolar clearing. In this regard, WHO recommends immunohistochemical demonstration of FH loss and/or 2-succinocysteine expression.

ChRCC is mostly sporadic, but can also be associated with Birt-Hogg-Dubé syndrome, in which the individuals have fibrofolliculoma, pulmonary cysts and bilateral multifocal renal tumours. Most ChRCC have a favourable outcome with partial nephrectomy recommended for small renal tumours. Risk of metastasis is low, but there is evidence that ChRCC has a predisposition to metastasize to the liver and lung.

Distinguishing renal oncocytoma (RO) and clear cell renal cell carcinoma (CCRCC) from ChRCC can pose a diagnostic dilemma when tumour cells show eosinophilic cytoplasm. ChRCC, especially the eosinophilic type, can be mistaken for RO, owing to the small cell size, eosinophilic granular cytoplasm and nested arrangement. The classic ChRCC as in our case are more easily distinguishable by virtue of their arrangement in sheets, with cells having prominent borders and finely reticulated cytoplasm. A characteristic feature of ChRCC is the presence of raisinoid hyperchromatic nuclei with perinuclear halo, as opposed to the round uniform nuclei of RO. Immunohistochemically ChRCC is frequently positive for CK7 and CD117. RO are typically positive for CD117, but CK7 negative. Another way to differentiate is by use of Hale's colloidal iron, which shows diffuse cytoplasmic staining in ChRCC as against RO which shows focal positivity confined to luminal borders.

The characteristic nuclear features along with the absence of cytoplasmic clearing and lack of a zonal pattern or thin fibrovascular septa helped rule out CCRCC from our differential diagnoses. Also, CCRCC is both CD117 and CK7 negative.

Renal LMS usually has an aggressive biological behaviour and occur in the elderly with poor prognosis. It can have atypical presentations or features mimicking the symptoms of other renal malignancies. Moazzam et al reported a case of renal LMS presenting with spontaneous retroperitoneal haemorrhage.[9] Sevilla et al reported a case of renal LMS in a 16 year old adolescent with tuberous sclerosis.[10] Darlington et al reported a case of renal LMS in a young female with malignant hypertension.[11]

Sarcomatoid carcinoma of the kidney is an important differential diagnosis to be considered. It often shows a malignant epithelial component, in contrast to the uniform fascicular architecture of LMS. Immunohistochemistry can aid in the diagnosis as sarcomatoid carcinoma is typically positive for cytokeratin and negative for actin, while the reverse is true for LMS.

Renal LMS also needs to be distinguished from renal epithelioid angiomyolipoma (EAML). Absence of mature adipose tissue and lack of thick hyalinized blood vessels, along with negative staining for HMB45 and S100 ruled out EAML from our differentials.

Renal LMS has a poor prognosis with median survival ranging from 17.9 to 25 months reported by Valery et al.[12] It should be considered in the differential diagnosis of renal masses particularly in elderly women, however there can be atypical presentations. In case of a high clinical suspicion of malignancy, radical nephrectomy should be advocated in such patients.

CONCLUSION

These renal neoplasms pose diagnostic challenges due to morphological overlapping, and similar presentations. Pathologists must consider the entire spectrum of differential diagnosis and use immunohistochemistry as an aid wherever necessary. Being aware of such presentations and findings can broaden our understanding of these renal tumours which can help in early accurate diagnosis for better outcome of the patient.

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