ORIGINAL RESEARCH PAPER

Volume-8 | Issue-6 | June-2019 | PRINT ISSN No. 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MORPHOLOGICAL SPECTRUM OF MALIGNANT RENAL TUMOURS IN DIFFERENT AGE GROUPS - CASE SERIES AND REVIEW OF LITERATURE

Pathology

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ABSTRACT

Renal tumours have acquired a new face in the recent times due to the expanding list of new entities. Renal cell carcinoma are classified based on their architectural features (eg: papillary RCC), cytoplasmic features (eg: clear cell and chromophobe renal cell carcinomas RCCs), anatomic location of tumours (eg: collecting duct and renal medullary carcinomas), and background in which they arise (eg: acquired cystic disease associated RCCs) , based on molecular changes (eg: MiT family translocation carcinomas and succinate dehydrogenase [SDH]–deficient renal carcinomas) or familial predisposition syndromes (eg: hereditary leiomyomatosis and RCC [HLRCC] syndrome–associated RCC). This article provides an insight into the various new entities and difficulties encountered in the diagnosis.

KEYWORDS

renal, carcinoma, mucinous, translocation, spindle cell

INTRODUCTION:

Renal tumours have acquired a new face in the recent times due to the expanding list of new entities. Renal cell carcinoma can be classified into different types based on histopathology, immunohistochemistry and the various molecular translocation associated with each subtype. WHO 2016 has classified them malignant renal tumours based on the various features as described above. It is important to subtype renal cell carcinoma because few subtypes of renal cell carcinomas are associated with a indolent course and helps in deciding the treatment protocol. This article provides an insight into the various new entities and difficulties encountered in the diagnosis.

METHODS:

This study is a prospective study involving different types of renal tumours received over a period from July 2017 to July 2018.

This is a case series, so we chose to describe each type of renal cell carcinoma received during this study period in Histolab, Coimbatore.

CASE SERIES:

CASE 1:

54 year old male right radical nephrectomy. Gross examination showed a tumour measuring with a variegated cut surface. Histology proved to **be conventional renal cell carcinoma**, histology grade 1-2, pT1bNx (Fig 1&2)

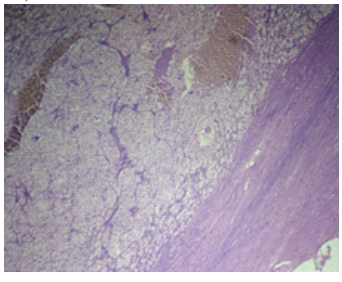

Fig: 2Fig: 1 – Conventional Renal cell Carcinoma (4x)

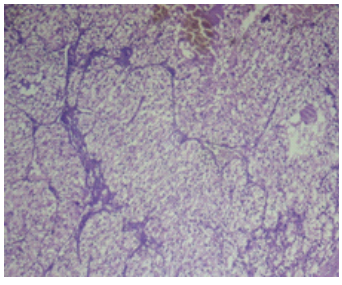

Fig: 2 – Conventional Renal cell Carcinoma (10x)

CASE 2:

48 year old male, left radical nephrectomy, sectioning showed a tumor measuring 15x10x6.6cm with a variegated cut surface. Histology **was conventional clear cell renal cell carcinoma with cystic change**, grade pT1bNx

CASE 3:

49 year old female left radical nephrectomy 9.5x8.5x7.5cm. Gross examination showed a homogenous tan cut surface. Biopsy proved to be **Eosinophilic variant of RCC, Fuhrman grade 2.** (Fig: 3&4)

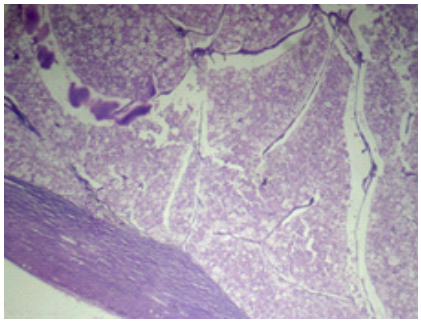

Fig: 3 – Eosinophilic variant of Renal cell carcinoma (4x)

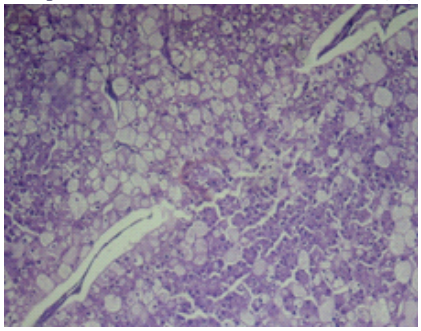

Fig: 4 - Eosinophilic variant of Renal cell carcinoma (100x)

CASE 4: Fig: 1619 year old female presented with right sided flank pain. Investigations revealed a mass in right kidney – malignant renal neoplasm. Right radical nephrectomy was done with removal of paracaval nodes. Gross examination sowed a partially circumscribed tumour measuring 10.5x.8x6.5cm with a tan cut surface. Histology showed a tumour arranged in nests with cells having a raisinoid nuclei and abundant eosinophilic cytoplasm. A diagnosis of chromophobe renal cell carcinoma, pT2b was favoured and advised immunohistochemistry.

CASE 5:
75 year old male left radical nephrectomy, gross examination revealed an unifocal tumour measuring 15x14x11cm in the lower pole of the kidney with a tan cut surface.

Histology showed **papillary renal cell carcinoma, type I** with20% necrosis, grade 1-2, pT2bNx. (Fig 5&6)

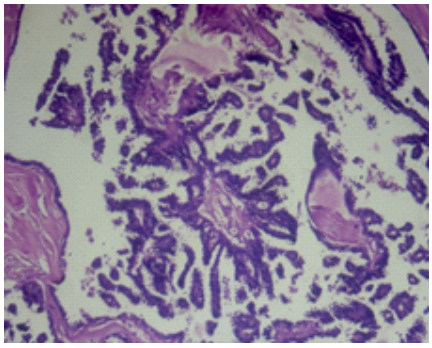

Fig: 5- Papillary renal cell carcinoma type I (4x)

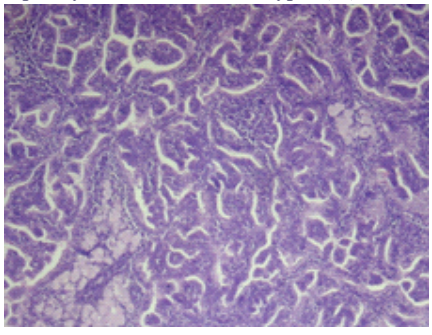

Fig: 6 – Papillary renal cell carcinoma type II (10x)

CASE 6:
58 yr old female, right radical nephrectomy was done and showed a tumour measuring 17x12x11.5cm. Sectioning showed a unifocal tumour involving the cortex and medulla, measuring 10.5x10.5x8.5cm, soft to firm with a tan cut surface.

Histology showed **mucinous areas and spindle cell** areas with 10% necrosis. Hilar resection margin was free of tumor. Fuhrmann nuclear grade was and stage was pT2bNx (Fig 7-10)

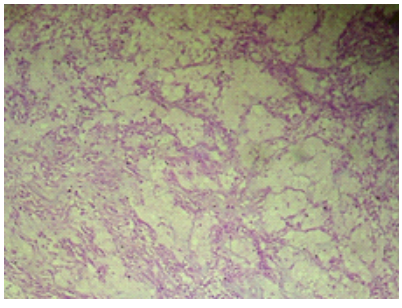

Fig: 7 – Mucinous areas in Mucinous tubular and spindle cell carcinoma (4x)

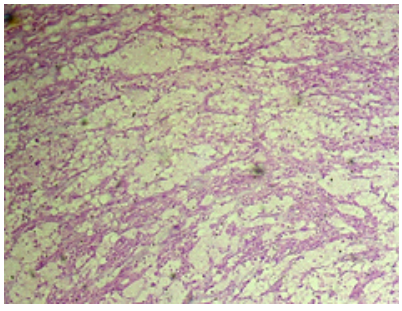

Fig: 8 - Mucinous areas in Mucinous tubular and spindle cell carcinoma (4x)

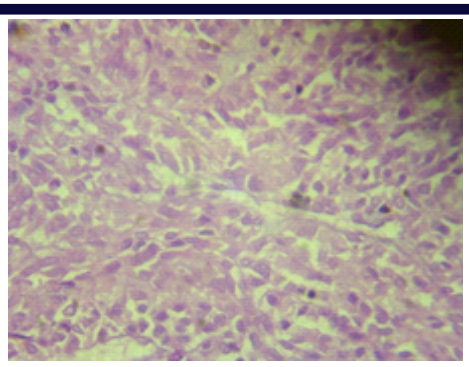

Fig: 9 – Spindle cell areas in Mucinous tubular and spindle cell carcinoma (4x)

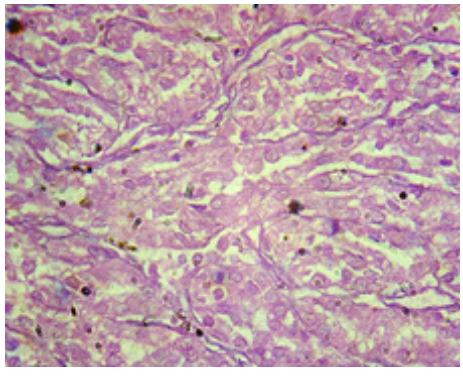

Fig: 10 - Tubular areas in Mucinous tubular and spindle cell carcinoma (4x)

CASE 7:
77 year old male presented with history of right sided flank pain. Investigations revealed a tumour in the right kidney. Gross examination showed an encapsulated tumour in the upper pole of the kidney measuring 4x3.5x2.5cm with multiloculated cyst containing jelly like haemorrhagic material.

Histology showed multiple cysts lined by columnar cells with clear cytoplasm and vesicular nuclei. A diagnosis of **Multilocular cystic renal neoplasm of low malignant potential ,** fuhrman grade 1-2, pT1a was made. (Fig: 11-13)

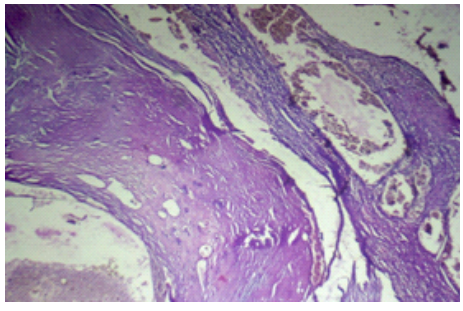

Fig: 11- Multilocular cystic renal neoplasm of low malignant potential (4x)

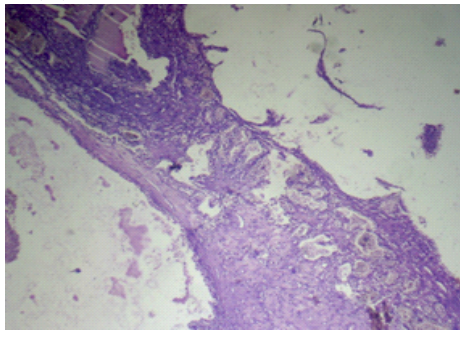

Fig: 12 - Multilocular cystic renal neoplasm of low malignant potential (10x)

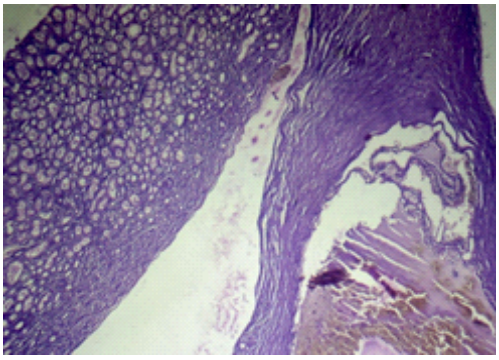

Fig: 13 - Multilocular cystic renal neoplasm of low malignant potential (100x)

CASE 8:
19 year old girl presented with c/o ABDOMINAL MASS.
Right radical nephrectomy with excision of paracaval nodes was done.

Gross examination showed a tumour measuring 10.5x8x6.5cm occupying the middle and the lower pole with firm cut surface and variegated appearance (Fig 14-16). Histopathological examination showed papillary areas, CK, PAX8, CD10, vimentin, TFE3, AMACR, EMA, SMA was negative. HMB45 & Melan A was positive. (Fig 14-16)

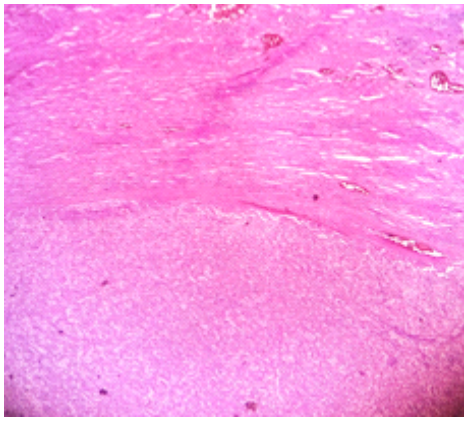

Fig: 14 – Transitional cell carcinoma (4x)

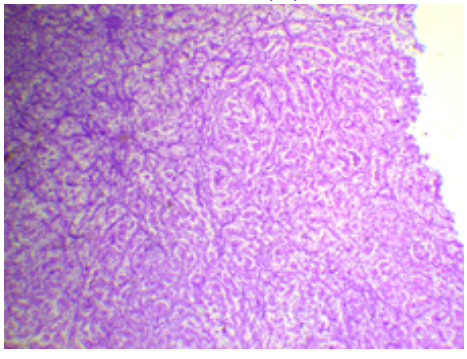

Fig: 15 – Nested pattern in Transitional cell carcinoma (10x)

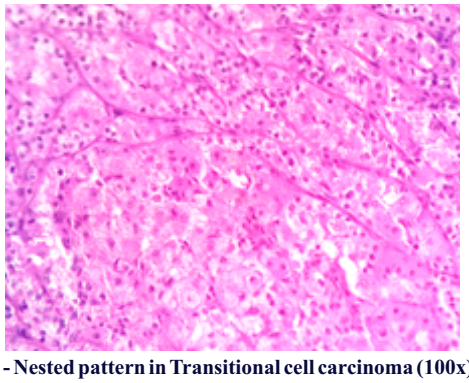

Fig: 16 - Nested pattern in Transitional cell carcinoma (100x)

DISCUSSION:
Renal cell carcinomas generally constitutes ~ 1-3% of all malignant visceral neoplasms[1]. The 2016 WHO classified renal cell carcinoma into various types like

- Clear cell renal cell carcinoma
- Multilocular cystic renal neoplasm of low malignant potential
- Papillary renal cell carcinoma
- Hereditary leiomyomatosis and renal cell carcinoma associated renal cell carcinoma
- Chromophobe renal cell carcinoma
- Collecting duct carcinoma
- Renal medullary carcinoma
- MiT family translocation renal cell carcinomas
- Succinate dehydrogenase deficient renal cell carcinoma
- Mucinous tubular and spindle cell carcinoma
- Tubulocystic renal cell carcinoma
- Acquired cystic disease-associated renal cell carcinoma
- Clear cell papillary renal cell carcinom
- Renal cell carcinoma, unclassified
- Papillary adenoma
- Oncocytoma[2]

Areas of evolving renal cell carcinoma includes transcription elongation factor B subunit 1 (TCEB1)– mutated RCC/RCC with angioleiomyoma-like stroma/ RCC with leiomyomatous stroma, RCC associated with anaplastic lymphoma receptor tyrosine kinase (ALK) gene rearrangement, thyroid like follicular RCC and RCC in neuroblastoma survivors.

Newly recognized epithelial renal tumours in the 2016 WHO classification are HLRCC-associated RCC, SDH-deficient RCC, tubulocystic RCC, acquired cystic RCC, and clear cell papillary RCC. Renal cell carcinoma is uncommon in young adults.

Radical nephrectomy is one of the common surgical procedure done for neoplastic and non neoplastic lesions. Histopathological diagnosis is very important and plays an important role in prognostication. Each subtype of renal cell carcinoma is associated with a different prognosis ranging from indolent course to those with poor prognosis. Here we present a case series of different types of malignant renal tumours in different age groups.

Grading of renal cell carcinoma is by ISUP grading taking into consideration the presence of nucleoli.[3](Table:1)

Table:1 (Grading of renal cell carcinoma)

GRADE	DESCRIPTION
Grade 1	Absent/inconspicuous nucleoli and basophilic at x400 magnification
Grade 2	Conspicuous nucleoli and eosinophilic at x400 magnification and visible but not prominent at x100 magnification
Grade 3	Conspicuous eosinophilic nucleoli at x100 magnification
Grade 4	Marked nuclear pleomorphism. Presence of multinucleate giant cells, sarcomatoid areas or rhanbdoid differentiation

CONVENTIONAL CLEAR CELL RENAL CARCINOMA:
Conventional clear cell renal carcinoma is the most common type of renal carcinoma. They constitute about 75% of the renal cell carcinoma. 95% of the cases are sporadic. The remaining 5% of cases may be syndromic association especially Von Hippal Lindau syndrome and tuberous sclerosis. [4] It originates from proximal nephron. Grossly, they have a variegated cut surface.

Histology shows nests of large cells with clear cytoplasm separated by delicate fibrovascular septae. Areas of haemorrhage, necrosis, cysts and calcification can be seen.[5] Clear cell carcinoma can show cystic change and eosinophilic change of the lining epithelial cells.

PAPILLARY RENAL CELL CARCINOMA:
Papillary renal cell carcinoma constitutes around 10% of renal cell carcinoma. They have an assocaition with Hereditary renal papillary carcinoma. Papillary renal cell carcinoma arises from the distal nephron. There are of two types.

Type 1 papillary renal cell carcinoma is characterized by the presence of small basophilic cells with scant cytoplasm.

Type 2 papillary renal cell carcinoma is characterized by the presence of cells with abundant eosinophilic granular cytoplasm.[6]

CHROMOPHOBE RENAL CELL CARCINOMA:
Chromophobe renal cell carcinoma arises from the distal nephron or intercalated cells of distal tubules and constitutes around 5% of the renal cell carcinoma.They have an association with Bird Hugg Dube syndrome. Chromophobe renal cell carcinoma shows a characteristic histology. They have large pale cells with raisinoid nuclei and perinuclear halo. Hales colloid l iron is usually positive in cases of Chromophobe renal cell carcinoma. Oncocytoma is a close diferential diagnosis for Chromophobe renal cell carcinoma.[7]

COLLECTING DUCT CARCINOMA:
Collecting duct carcinoma arises from the collecting tubules. They are characterized by irregular infiltrating cells with marked desmoplasia.[8]

MEDULLARY CARCINOMA:
Medullary carcinoma arises from the distal nephron. They have a strong association with sickle cell disease/trait. Medullary carcinoma usually occurs at young age especially in the 2-3rd decade.[9]

Xp11 Translocation Associated Renal Celcarcinoma:
They are rare types of renal cell carcinoma characterized by the presence of TFE3 mutation. [10]

Translocation associated RCC usually occurs in young adults and children and is histologically characterised by nested architecture. Papillary and clear cell morphology with abundant cytoplasm and well defined borders can also be seen. Translocation associated renal cell carcinoma can be either one of the following two types

ASPL-TFE3 : Abundant cytoplasm and psammoma bodies, high grade nuclear features or
PRCC-TFE3 : Less cytoplasm, less psammoma bodies

Rearrangements in MiT transcription factor- TFE3/TFEB are usually seen in translocation associated RCC leading to nuclear positivity for TFE3 which can be detected immunohistochemically

The differential diagnosis of translocation associated RCC includes
- Clear cell RCC
- Clear cell papillary RCC
- Papillary RCC type 2
- Epithelioid angiomyolipoma

Renal cell carcinoma in a person less than 30 years with characteristic morphology and cytokeratin negativity should raise the possibility of translocation associated RCC.

MUCINOUS TUBULAR AND SPINDLE CELL CARCINOMA:
They are very rare types of renal cell carcinoma.[11] This tumour was first recognized by MacLennan et al in 1997 and reported as "low-grade mucinous tubulocystic carcinoma of possible collecting duct origin," This tumour has slight female preponderance.

Immunohistochemically, MTSCC expresses markers of both distal (CK7) and proximal tubular (RCC Ma, AMACR, CD15) differentiation. The main differential diagnosis of MTSCC is sarcomatoid papillary RCC (PRCC).

MULTILOCULAR CYSTIC RENAL CELL CARCINOMA:
They constitute only around 1-4% of all renal cell carcinomas. They are characterized

histologically by the presence of multiple cysts with the septae containing malignant cells. They are generally associated with good prognosis. M*ultilocular cystic renal neoplasm of low malignant potential* is now the WHO-recommended term for multilocular cystic RCC as they were not associated with recurrence or metastasis. *Multilocular cystic renal neoplasm of low malignant potential* is characterized by numerous cysts with low-grade tumour cells (WHO/ISUP grade 1 or 2). The cysts are lined by a single layer of tumour cells with abundant clear cytoplasm. The septa contain clear cells but without expansile growth.[12]

CONCLUSION:
As we can see from the case series, most of the patients have same clinical features and gross appearance of the tumour. So, histological examination along with immnuohistochemistry becomes necessary in exact diagnosis and typing of renal cell carcinoma for proper prognostication. Sometimes, molecular methods have to be employed for diagnosis of tumours like translocation associated renal cell carcinoma. To conclude, morphology, histopathology, immunohisto chemistry and molecular methods deployed together can help in the correct diagnosis and prognosis of renal tumours.

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