

Histopathologic Spectrum of Adult Renal Epithelial Tumors in a Tertiary Care Hospital in India

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ABSTRACT

40 cases of adult renal epithelial neoplasms received at Saifee Hospital, Mumbai for a period of 3 years were evaluated for various gross and microscopic features. Demographic details and histopathologic prognostic determinants were studied for all the cases. All 40 cases studied were malignant neoplasms. A male predominance (3:1) and predilection for left kidney (60%) were observed. Majority of the cases were between 41-70 years age. Conventional clear cell RCC was the commonest histologic subtype (67.5%), followed by Papillary RCC (17.5%) and Chromophobe RCC (10%). Only one case of Multilocular cystic RCC and one very rare case of unilateral synchronous clear cell RCC with papillary RCC were encountered. Furhman nuclear grade 2 was the commonest (60%), followed by grade 3 (27.5%) and grade 4 (12.5%). Necrosis was identified on microscopy in 50% cases and 5% cases showed sarcomatoid features. Lymphovascular invasion was present in 12.5% cases and Hilar lymph node metastases in 10% cases.

Keywords: Histopathologic Spectrum, Renal, Epithelial, Tumors

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INTRODUCTION

Renal tumors establish a heterogenous gathering of neoplasms recognizable histologically and cytogenetically. Renal tumors represent 3% of every single harmful tumor and 2% of by and large cancer mortality.¹ While the specific reason for renal cancer stays obscure, reported hazard factors incorporate cigarette smoking, corpulence, hypertension, diabetes, estrogen treatment, word related introduction to oil based commodities, substantial metals, asbestos, interminable dialysis and renal failure.² Renal neoplasms are overwhelmingly inconsistent. All things considered, innate neoplasms demonstrating relationship with autosomal predominant issues like Von Hippel Lindau Disease, Birt Hogg Dube Syndrome have been accounted for. Immunohistochemistry can possibly separate between various subtypes of essential renal neoplasms. Antibodies like CA IX, CK 7, C Kit, racemose and CD 10 have ideal viability. The far reaching utilization of stomach ultrasound and CT as insightful devices for some nonurological protests prompted a sensational increment in discovery of little asymptomatic coincidental renal masses.³ Currently, better comprehension of atomic hereditary qualities has brought about some energizing advancement in the administration of renal neoplasms. Reports show that these tumors are predominantly of epithelial origin and majority are renal cell carcinomas. They have relatively distinct patterns.⁴

MATERIAL AND METHODS

Our aim was to study the histopathological features of renal epithelial tumors in adults in a tertiary care hospital in Mumbai for a period of 3 years. We aimed to study frequency of various adult renal epithelial neoplasms along with their

gross, microscopic and immunohistochemical features. An approval from Institutional ethical Committee was taken.

Inclusion criteria

- 1) Specimens of patients over 16 years of age were included.
- 2) Only 'epithelial' renal neoplasms were included.
- 3) Only partial, complete or radical nephrectomy specimens were included.

The specimens were examined carefully and gross features were noted. The specimens were fixed in 10% neutral buffered formalin. Representative sections were submitted for paraffin processing and later stained with hematoxylin and eosin stains for microscopic evaluation.

OBSERVATIONS

Total 40 cases of surgically resected renal tumors received in a period of three years were analysed. All the lesions were malignant and none was benign. Out of 40 cases, the majority cases i.e.33 (82.5%) were radical nephrectomy. 5 (12.5%) cases were complete nephrectomy, one (2.5%) was nephroureterectomy and one (2.5%) was partial nephrectomy. There was a male predominance with male to female ratio of 3:1. Renal epithelial tumors occur most commonly in 40 – 70 years age group. In our study, majority of the cases were between 41 – 70 years age, accounting for 75% of cases (Table 1). Lowest incidence was found in 16 – 30 years age group (5%). The youngest patient was 29 years old and the eldest was 77 years, in this study. Majority of tumors were located on left side (60%). Relatively a smaller number of tumors were on right side (40%). There were no bilateral tumors in this study.

Table 1: Age distribution of Adult Renal Epithelial Tumors

Age (years)	No. of cases	Percentage (%)
16 – 30	02	5%
31 – 40	03	7.5%
41 – 50	12	30%
51 – 60	10	25%

61 – 70	08	20%
71 – 80	05	12.5%
Total	40	100%

Table 2: Distribution according to histologic type of tumors

Histologic type	No. of cases	Percentage (%)
Conventional clear cell RCC	27	67.5%
Papillary RCC	07	17.5%
Chromophobe RCC	04	10%
Multilocular cystic RCC	01	2.5%
Synchronous Conventional RCC with papillary RCC	01	2.5%
Total	40	100%

All the tumors encountered were malignant and none was benign. All the cases were RCCs of various histologic subtypes. Conventional clear cell RCCs accounted for 67.5% of the cases, consisting the majority among all subtypes (Table 2). In the remaining cases, papillary RCCs were relatively common with percentage of 17.5%. Chromophobe RCCs were less common with 10% cases. Only one case of multilocular cystic RCC and one case of synchronous conventional clear cell RCC with papillary RCC were encountered. Among papillary RCC cases, 5 cases were type 2 and remaining 2 cases were type 1. On gross examination, the conventional RCCs were partially circumscribed, unifocal and golden yellow in colour (Image 1). Tumor size ranged from 2.5cm to 9cm. Necrosis was noted in 6 cases, cystic change in 4 cases (Image 2) and hemorrhage in 5 cases. Extension into renal sinus and perinephric fat was present in 13 cases.

Papillary RCCs were ill circumscribed and yellowish white with tumor size ranging from 2.7cm to 23cm. In one case, tumor was a unilocular cyst with intraluminal grey brown friable mass. Yellowish white fleshy appearance was observed in two cases. Necrosis was noted grossly in one case. In one case of papillary RCC type 2, the tumor was bosselated, irregular, yellowish white fleshy measuring 23 x 18 x 13cm. The tumor replaced almost entire renal parenchyma with extension into renal sinus, perinephric fat and renal vein (Image 3). Majority of chromophobe RCCs were fairly circumscribed, solid, tan brown tumors with size ranging from 6.5 cm to 19.5 cm. In one case, the tumor was yellowish white and partly necrotic measuring 19.5x11x9 cm. This tumor was associated with sarcomatoid features on microscopy. It also showed extension into renal sinus and perinephric fat.

The multilocular cystic clear cell RCC measuring 4.4x4.3x3 cm had cystic spaces containing hemorrhagic fluid (Image 4). The inner surface of the cysts had golden yellow trabeculated appearance. In case of unilateral synchronous RCC, grossly there were two tumors in the same kidney. The larger tumor was located at upper pole and it had golden yellow appearance. A grey white satellite tumor nodule measuring 1 x 0.8 x 0.7 cm was noted 4.2 cm inferior to larger tumor (Image 5). Microscopically, there were two synchronous tumors with larger being conventional clear cell RCC and smaller satellite nodule being papillary RCC.

The conventional clear cell RCCs comprised predominantly of cells with clear cytoplasm, although foci of cells with

eosinophilic cytoplasm were encountered. They showed a characteristic delicate, branching vasculature and had solid and cystic architectural patterns (Image 6). Rhabdoid features were noted on microscopy in one case of conventional clear cell RCC (Image 7). This case had Furhman nuclear grade 4. Also, this tumor showed extension into renal sinus and renal vein and metastasis to supraclavicular lymph node.



Image 1: Gross appearance of Conventional clear cell RCC. Tumor is ill circumscribed and is golden yellow in color.



Image 2: Gross appearance of Conventional clear cell RCC showing golden yellow tumor with areas of necrosis and cystic change.



Image 3: Papillary RCC grossly invading the renal sinus. The tumor is grey white fleshy and is almost entirely replacing the renal parenchyma.



Image 4: Gross appearance of Multilocular cystic RCC showing multicystic tumor with cysts containing hemorrhagic fluid.



Image 5: Unilateral Synchronous Conventional clear cell RCC and Papillary RCC. Grossly showing a larger tumor (CRCC) is golden yellow with interspersed whitish areas and a smaller grey white tumor (Papillary RCC).

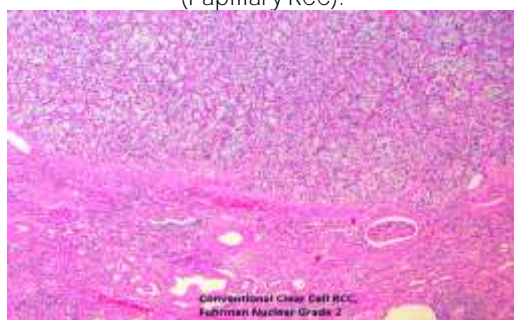


Image 6: 40X magnification view of Conventional clear cell RCC with adjacent renal parenchyma.

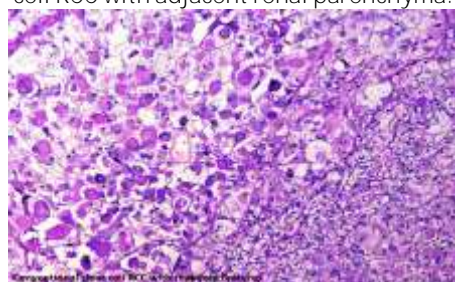


Image 7: 100X magnification view of Clear cell RCC with Rhabdoid features.

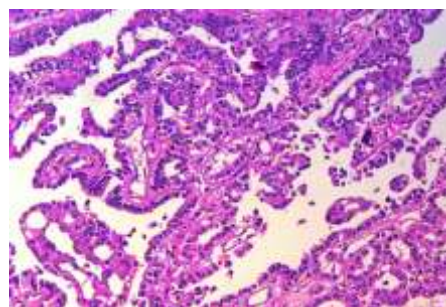


Image 8: 100X magnification view of Papillary RCC type 2.

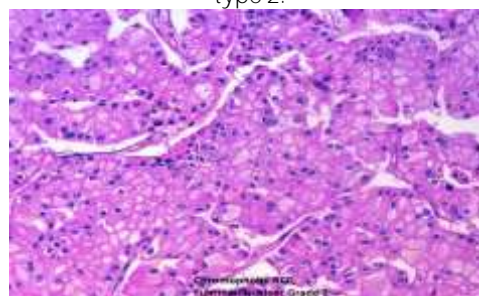


Image 9: 100X magnification view of Chromophobe RCC.

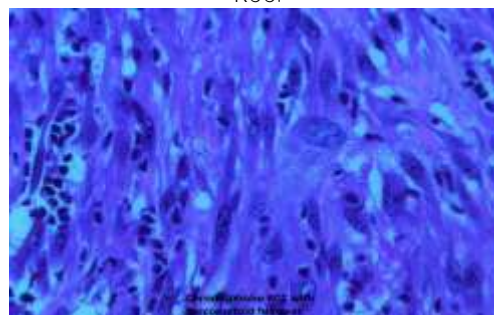


Image 10: 400X magnification view of Chromophobe RCC with Sarcomatoid features.

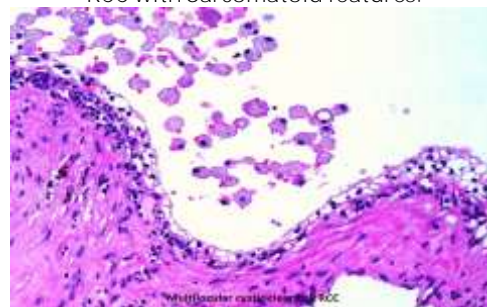


Image 11: 100X magnification view of Multilocular cystic RCC.



Image 12: Cytokeratin 7 positivity exhibited by Papillary RCC in case of unilateral Synchronous CRCC with Papillary RCC.

One case of conventional clear cell RCC showed sarcomatoid features. Furhman nuclear grade in conventional areas was G3. Sarcomatoid areas showed spindle to round cells with pleomorphic hyperchromatic nuclei.

In type 1 papillary RCC cases, cells were small with inconspicuous pale cytoplasm. Nuclei were uniform, spherical and small with small or invisible nucleoli. In type 2 papillary RCC tumors, nuclei were arranged in a pseudostratified pattern. The nuclei were large and spherical with prominent nucleoli (Image 8).

Microscopically, the growth pattern of Chromophobe RCC was predominantly solid, at times tubulocystic, with broad fibrotic septae. Tumor cells were large, polygonal with abundant transparent to granular eosinophilic cytoplasm and prominent cell membranes (Image 9). Binucleation and perinuclear halos were commonly observed. One case of chromophobe RCC had sarcomatoid features with Furhman nuclear grade 4 (Image 10). Sarcomatoid areas showed many mitoses, bizarre nuclei and few tumor giant cells. Hilar lymph node metastasis in this case showed only sarcomatoid areas. Microscopically, the cysts in multilocular cystic RCC were lined by cuboidal cells with clear cytoplasm and low grade nuclei (nuclear grade G2). Small groups of tumor cells were also noted in fibrous septae (Image 11).

Furhman nuclear grade 2 was commonest, which was present in 24 cases (60%). Furhman nuclear grade 3 was noted in 11 cases (27.5%) and grade 4 was noted in 5 cases (12.5%). Furhman nuclear grade 1 was not found in the cases studied. Necrosis was identified on microscopy in 50% of cases. Necrosis was present in 15 cases of conventional clear cell RCC, 5 cases of papillary RCC and 1 case of chromophobe RCC. Sarcomatoid features were found in 2 (5%) cases. Out of these 2 cases, one was conventional clear cell RCC and other was chromophobe RCC.

Lympho-vascular tumor invasion was seen in 5 cases (12.5%), of which 3 cases (7.5%) showed extension into renal vein. Metastasis to Hilar lymph nodes was found in 4 cases (10%) and only one case showed distant metastasis to supraclavicular lymph node.

Immunohistochemistry was performed in 2 cases. In one case, there was synchronous presence of conventional clear cell RCC and papillary RCC. Cytokeratin 7 positivity in tumor cells of papillary RCC was demonstrated in this case (Image 12). In second case, the histologic type of tumor was papillary RCC type 2. Tumor cells expressed pancytokeratin and vimentin.

Table 3: Pathologic staging of tumors

Pathologic stage	No. of cases	Percentage (%)
Stage I	15	37.5%
Stage II	06	15%
Stage III	16	40%
Stage IV	03	7.5%
Total	40	100%

Among the cases studied, maximum were stage III tumors with 16 cases (40%). These cases had either renal sinus involvement or invasion into perinephric fat. 3 cases (7.5%) were stage IV, of which one case had tumor infiltration in adrenal gland, other had involvement of skeletal muscle after invasion of Gerota's fascia and third case had metastasis to supraclavicular lymph node. Stage I tumors account for 15 cases (37.5%), where tumor was limited to kidney with size of less than 7 cm. Stage II tumors were 6 (15%) (Table 3). In stage II cases, tumor was limited to kidney with size more than 7 cm.

Hilar lymph node metastasis was found in 4 (10%) cases. Out of these 4 cases, 2 cases were of papillary RCC type 2, one case was of conventional clear cell RCC and one of chromophobe RCC. Distant metastasis was present in only 1 case (2.5%), which was clear cell RCC with rhabdoid features, where tumor metastasis was found in supraclavicular lymph node.

DISCUSSION

Primary renal tumors comprise a wide spectrum of neoplastic lesions of kidney with patterns which are relatively distinct among children and adults. Renal cell carcinoma is the most common malignancy of adult kidney with a variable outcome. Currently, tumor size, RCC subtype, nuclear grade and tumor stage are widely accepted as prognostic indicators.⁵ In present study, we aimed to determine

histopathological features of adult renal epithelial tumors in a tertiary health care centre.

We did not find any benign tumor of kidney, all the tumors encountered during study period were malignant. The frequencies reported by Amin et al⁶ and Park et al⁷ were closest to our frequency.

In the present study, the age of the patient ranged from 29 years to 77 years with mean age of 53 years. The mean age in our study is slightly lower than mean age of 60 years reported by Best et al⁸, 57 years reported by Grignon et al⁹ and Pradhan et al¹⁰.

The renal cell carcinoma was more common in males with M:F ratio 3:1 in the present study. The male preponderance is concordant with the findings of all other authors.

The tumour was noted in right kidney in 16 cases and in left kidney in 24 cases with R:L ratio of 2:3. However, predilection for right side was noted by Best⁸ with R:L ratio of 2:1.

Conventional clear cell RCC accounted for maximum number of cases in this study (67.5%). Similarly, in the series of Grignon et al⁹ (74.76%), Kim et al¹¹ (86.3%) and Gudbjartsson et al¹² (88.7%), clear cell type tumour was the commonest.

Grossly, the affected kidneys in Conventional clear cell RCC were enlarged and cut section showed typical golden yellow appearance of the tumour. Similar findings were reported by Said J et al¹³. Most of the tumours in this study measured 5

to 10 cms in size which correlates with tumour size of 8.6 +/- 3.4 cms reported by Fauzia et al¹⁴.

In majority of cases (53.33%), the tumour cells were arranged into a mixed pattern consisting of solid (sheets and clusters), acinar and tubular patterns. Predominant solid pattern was noted in 20% of cases, while acinar and papillary patterns were observed in 13.33% cases each. In study done by Reis and Faria¹⁵, solid pattern was the commonest accounting for 40.7% and mixed pattern in 9.8% of cases.

The frequency of papillary RCC in this study (17.5%) coincides with 14.03% frequency observed by Mancilla-Jimenez et al¹⁶. All other studies showed lower frequency of papillary RCC. Microscopically, the tumour showed predominant papillary pattern. The papillae were lined by cuboidal to columnar cells having pleomorphic vesicular nuclei with prominent nucleoli and abundant eosinophilic cytoplasm. These characteristic features are in accord with findings of Mancilla-Jimenez et al¹⁶ and El-Naggar et al¹⁷.

The frequency of chromophobe RCC (10%) is higher than frequency found by Cheville et al¹⁸ (4.3%) and Patard et al¹⁹ (2.6%). In a 10 year study carried out in Memorial Sloan-Kettering cancer centre²⁰, the frequency of chromophobe RCC was 8%, which compares well with our study.

The true incidence of multilocular cystic RCC is unknown because no strict criteria were defined previously. Some reports suggest that cystic renal cell carcinomas (including multilocular cystic RCC, unilocular cystic RCC and RCC with extensive cystic necrosis) might represent 3% to 14% RCC.²¹ Overall, these tumors are rare and criterias laid by 2004 WHO classification of kidney tumors should be followed before labelling any case as multilocular cystic RCC. Our study includes a rare case of unilateral synchronous conventional clear cell RCC and papillary RCC. There are a few studies that define bilateral synchronous malignant renal tumors and coexisting benign and malignant tumors arising within same kidney. To the best of our knowledge, clear cell RCC and papillary RCC arising within same kidney are very rare in literature. Simhan et al²² reported data of 97 patients who had multifocal renal tumors. They reported 8 cases who had mixed papillary and clear cell RCC. Capaccio et al²³ found 7 cases who had unilateral synchronous tumors with different subtypes. Of these, 3 cases had synchronous papillary and clear cell RCC.

Invasion of renal capsule was noted in 11cases (27.5%) in the present study. This is in concordance with Selli et al²⁴ who observed it in 22.06% of cases.

The frequency of sarcomatoid features in RCC (5%) in present series is close to the frequency reported by Sella et al²⁵ and Oda and Machinami²⁶.

There is a significant correlation between tumor size and tumor grade with stage. Larger tumors are prone to have higher grade and stage.²⁷ Histologic grade is an independent factor correlating with survival.^{28,29} Multiple systems are used to grade RCC of which Furhman grade is most widely used.²⁹ We applied Furhman nuclear grade and grade 2 was the commonest (60%). This was similar to study by Atif et al.³⁰ According to Tsui et al, five year survival rate based on tumor grade was 89%, 65% and 46% for tumors with grade 1, 2 and 3 to 4 respectively.²⁸

Lympho-vascular tumor embolisation is a reliable prognostic marker with high risk for development of metastatic disease.³¹ We found a notable frequency of 12.5% in our study, which is similar to study done by Stinga et al.³²

Study by Abel et al³³ found that extent of vena caval invasion was an important prognostic factor and indicator of recurrence rate. Our study had 7.5% cases with renal vein invasion, which was comparable to study by Atif et al³⁰ and Bocordo et al³⁴ (10%).

Adrenal gland involvement makes prognosis of RCC patients worse than perirenal fat invasion.^{35,36} Direct ipsilateral adrenal gland involvement is rare to occur. In our study, there was only one case (2.5%) of adrenal gland involvement. Kobayashi et al³⁷ and Atif et al³⁰ found 3% and 2% cases of adrenal gland involvement, respectively.

CONCLUSION

Adult renal tumors are heterogenous in nature and majority of them are malignant. The gold standard in treatment is partial or radical nephrectomy. A careful histopathological examination is crucial to evaluate histologic subtype and various other prognostic determinants. Most of the times, the gross and microscopic features correlate well with the stage and outcome of the patient and hence, a meticulous histopathologic evaluation should be emphasised while handling nephrectomy specimens.

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