"Clinicopathological study of adult renal tumours"

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Abstract

Introduction: A wide variety of both benign and malignant tumours arise from different components of the renal parenchyma, notably tubular epithelium. Prognostic markers for Renal cell carcinoma such as tumor stage, grade and necrosis are useful for determining appropriate follow-up and selecting patients for adjuvant therapy. We undertook this study to determine the relative frequencies of different types of adult renal tumours, their clinical, radiological, gross morphological and histopathological features. Our second objective was to evaluate these pathological variables and to establish possible correlations between them.

Materials and Methods: A Total of 60 Cases of adult renal neoplasms diagnosed at our institute from June 2007 to June 2014 were reviewed. Age, sex, histologic subtype, pT stage, Fuhrman grade, tumor necrosis were determined in all cases.

Results: Among 60 patients, 36 were males and 24 were females. Mean age was 46.5 years. 83.3% tumours were malignant and 16.67%, benign. Among malignant tumours, Renal cell carcinoma (RCC) was the commonest(78.3%). Various subtypes of RCC included: conventional/clear cell RCC (73.2%); papillary, (14.6%); chromophobe (2.4%) and RCC unclassified (1.66%). Other malignant tumours were: leiomyosarcoma (1.66%); spindle cell sarcoma (1.66%); primitive neuroectodermal tumour(1.66%). Benign renal tumours included Angiomyolipoma(10%), oncocytoma(1.66%); metanephric adenoma(1.66%) and renomedullary interstitial tumour (1.66%).

Conclusions: RCC was the commonest malignant tumor and conventional/clear cell RCC was the most common subtype. Most of the cases in our study were in grade 2 and stage pT3. Papillary RCC was second most common subtype.Tumor necrosis correlates with higher grade and tumor stage.

Key Words: Renal cell carcinoma, Furhman nuclear grade, Leiomyosarcoma, renomedullary interstitial tumour, Primitive neuroectodermal tumour.

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Introduction

Renal tumours comprise a diverse spectrum of neoplastic lesions with patterns that are relatively distinct for children and adults. A wide variety of both benign and malignant tumours arise from different components of the renal parenchyma, notably tubular epithelium.[1] Accurate diagnosis of most renal tumours is not possible before surgery and histopathological evaluation. A detailed and meticulous histopathological examination of tumour nephrectomy specimen is essential to establish histological type and to record accepted histopathological prognostic determinants i.e. tumour size, histological subtype, nuclear grade and stage in cases of malignant renal neoplasms. We undertook this study to determine the relative frequencies of different types of adult renal tumours, their clinical features, radiological features, gross morphological features, histopathological characteristics and to compare our findings with those in previously published literature.

Materials and Methods

A Total of 60 Cases of adult renal neoplasms diagnosed at our institute over a period of 7 years were reviewed.

Inclusion Criteria: All adult renal tumours – nephrectomies received in surgical pathology as well as renal tumours which were diagnosed at autopsy cases including

1. Renal cell tumours
2. Mesenchymaltumours
3. Neuroendocrine tumours.

Exclusion criteria: Renal tumours in patients below 18 years. Transitional cell carcinoma, squamous cell carcinoma and adenocarcinoma of renal pelvis were also not included in the study. Patient's demographic and clinical data were recorded from indoor paper.

The morphological data included tumour size, gross appearance of the tumour, extrarenal spread, histological subtype, pathological TNM stage and in cases of Renal cell carcinoma, Furhman nuclear grade was also studied.

At the time of primary reporting, nephrectomy specimens were received and fixed in 10% buffered formalin. After fixation, a note was made of weight, dimensions of kidney, length and diameter of ureter, gross description of tumour which included features like site, dimension, solid or cystic, invasion of capsule, perirenal tissue, calyces, renal vein renal artery, ureter

and presence of hemorrhage, necrosis and satellite nodules. 6-9 Representative tissue Sections were taken and processed by standard procedure. Slides were stained with haematoxylin and eosin (HandE) and Special stains like PAS, EVG were done in indicated cases.

WHO classification of renal neoplasms was employed for the diagnostic categorization of the tumours. Revised Tumour, Node, Metastases (TNM) classification 2002 was used for staging.

Fuhrman nuclear grading system was employed for grading the clear cell renal cell carcinoma. Each tumour was graded according to highest grade exhibited.

Results

A total of 60 renal tumours from 60 adult patients were analyzed. Mean age of patients was 46.2 years with majority of the patients in the age group of 41-60 years followed by 20-40 years. Of these, 36(60%) were males and 24 (40%) females. The male to female ratio was 1.5:1.

Majority of the patients in our study presented with Hematuria (28.3%) followed by flank pain (20%). Whereas classical triad of renal cell carcinoma was noted only in 05 patients (8.33%). In our study 08 cases 0f renal tumours were detected incidentally. Out of 8 cases, 02 cases were detected on autopsy and 06 cases were detected radiologically. Papillary RCC accounted for 37.5% of incidentally detected tumours followed by clear cell RCC accounting for 25% of cases.

Radiological diagnosis through CT scan was consistent with histopathology diagnosis in 92% cases whereas USG was consistent with histopathological diagnosis in 95% cases. Out Of 60 tumours, 83.3% tumours were malignantand 16.67% were benign. The histologic types and frequency distribution of these tumours is shown in Table 1.

Table 1: Histological subtypes of adult renal tumours

Histological Subtypes	Number of Cases	Percentage
Benign Tumours		
Angiomyolipoma	06	10%
Oncocytoma	02	3.33%
Metanephric Adenoma	01	1.66%
Renomedullary Interstitial Tumour	01	1.66%
Malignant tumours		
Renal Cell Carcinoma	47	78.33%
1. Clear Cell RCC	36	60%
2. Papillary RCC	08	13.33%
3. Chromophobe RCC	02	3.33%
4. RCC Unclassified	01	1.66%
Leiomyosarcoma	01	1.66%
Spindle Cell Sarcoma	01	1.66%
PNET	01	1.66%

Gross Features:

Table 2: Gross features of renal tumours

Gross Features	Renal Cell Carcinoma	Angiomyolipoma	Oncocytoma	Others	Total
Laterality					
Right kidney	25	06	01	03	35
Left kidney	21	--	01	02	24
Bilateral inv	01	--	--	--	01
Location of tumour					
Upper pole	13	01	01	03	18
Mid pole	10	01	01	--	12
Lower pole	10	02	--	--	12
Entire kidney	10	01	--	01	12
Half kidney	02	01	--	--	03
Pc, hilar	02	--	--	--	02
Medulla	--	--	--	01	01

Only one case of clear cell RCC showed bilateral involvement which was found to be associated with VHL syndrome.

The maximum diameter of tumour was that of spindle cell sarcoma (25x12x13cm) and smallest tumour was renomedullary interstitial tumour (2x2x2mm). Overall mean size of all the renal tumours was 7.5cm.

Grossly, Variegated appearance of tumour with areas of haemorrhage and necrosis along with cystic change was most commonly seen in Clear cell variant of RCC whereas majority of Papillary RCC were hemorrhagic with areas of necrosis.

Table 3: Extrarenal spread of renal cell carcinoma

Spread	Clear cell RCC	Papillary RCC	Chromophobe RCC	RCC unclassified	Total
Perinephric fat	06	01		01	08
Capsular invasion	06	02		01	09
Renal sinus	03	02	01		06
Pelvic calyceal system	05	02	01	01	09
Renal vein	08	02			10
Ureter	02				02
IVC	02	01			03
LN metastasis	02	03			05
Distant metastasis	Bone 01 Liver -02				03

Most common route of spread of renal cell carcinoma in our study was to the renal vein (21.2%) followed by pelvicaliceal sysyem(19%) and capsular invasion (19%).

Fuhrman's nuclear grading system was applied to 36 cases of CCRCC. The following table depicts grading:

Table 4: Grading of clear cell RCC

Grading	Clear cell RCC No. of Cases
Grade I	06
Grade II	23
Grade III	05
Grade IV	02

TNM staging was applied to renal cell carcinoma only in our study.

Table 5: Staging of renal cell carcinoma

Stage	Clear cell RCC	Papillary RCC	Chromophobe RCC	RCC unclassified	Total
Stage I	20	02	--	---	22
Stage II	03	01	--	---	04
Stage III	10	04	02	01	17
Stage IV	03	01	---	---	04

4 cases in our study presented in stage 4, out of which 3 were clear cell RCC and one was papillary RCC. 2 cases of stage IV clear cell RCC showed renal vein invasion, 2 cases showed liver metastasis and one case showed vertebral metastasis. Whereas the stage IV papillary RCC showed renal vein invasion along with lymph node metastasis.

2 cases of stage IV RCC showed IVC invasion, one of clear cell and one of papillary RCC. Thus indicating the most common route of spread of RCC in our study was through renal vein.

As is evident from the table, Clear cell RCC of low grade (grade I and grade II) mostly presented in stage I and stage II whereas High grade tumours (grade III and grade IV) presented in all the 4 stages.

Table 6: Staging vs grading of clear cell RCC

Stages	Grade I	Grade II	Grade III	Grade IV
I(N=20)	04	14	01	01
II(N=03)	01	01	01	---
III(10)	--	08	01	01
IV(03)	01	--	02	---
TOTAL(N=36)	06	23	05	02

Low grade Papillary RCC presented in stage I and stage II whereas High grade Papillary RCC presented in stage III and IV.

Table 7: Staging vs grading of papillary RCC

Stage	Low grade	High grade
I(N=02)	02	----
II(N=01)	01	---
III(N=04)	01	03
IV(N=01)	--	01

Discussion

The mean age of presentation in our study was 46.2 years which was comparable to other national and international studies(Latif et al[1] and Hashmi et al[2]). M:F ratio in our study was 1.5:1 but a female preponderance was noted in angiomyolipoma. Male preponderance was also noted in studies by Latif et al[1] and Hashmi et al[2]. Renal cell carcinoma usually presents with a classical triad of flank pain, hematuria and abdominal lump. In our study, classical triad was noted in 10.67% cases which was slightly higher than 4% as observed by Siddharth et al[3]. Hematuria and flank pain were observed in 31.9% and 19.1% cases respectively which was comparable to studies conducted by Siddharth et al[3] and Gupta et al[4]. In our study, 12.67% cases of RCC were incidentally detected. In the study conducted by Gupta et al[4], 10.6% of tumours were incidentally detected.

In our study, the malignant tumours vastly outnumbered the benign tumours. Malignant tumours accounted for 83.34% cases in our study which was similar to 82.37% cases in study conducted by Gupta et al[4]. Among the malignant tumours, Renal cell carcinoma was the most common (78.33%) Among the histological subtypes, Clear cell variant of RCC was the most common followed by Papillary RCC in our study.

The following table compares the incidence of various subtypres of RCC in different studies:

Table 8: Renal cell carcinoma – histological subtypes

Histological subtype	Siddharth et al [3] 2011 N= 50	Hashmi et al [2] 2014 N=50	Latif et al [1] 2011* N=41	Present Study 2015 N=47
Clear cell RCC	82%	62%	73.2%	76.5%
Multilocular cyst clear cell RCC	04%		---	---
Papillary RCC	14%	24%	14.6%	17%
Chromophobe RCC	--	06%	2.4%	4.25%
Sarcamatoid RCC	---	08%	9.7	----
RCC unclassified				1.66%

In our study, 53.1% 0f RCC involved the right kidney which was found to be comparable with Siddharth et al[3](52%) and Hartmann et al[5](51%). Bilateral involvement of the kidney in our study was found only in one case of clear cell RCC which was associated with Von Hippel–Lindau disease. Siddharth et al[3] had one case of bilateral RCC which was also associated with Von Hippel–Lindau disease. Upper pole was the most common location of RCC which was found to be similar to the observation by Siddharth et al[3].

The mean size of renal cell carcinoma in our study was 6.56 cm which was comparable to other studies by Latif et al[1] and Siddharth et al[3].

Most common route of spread of Renal cell carcinoma in our study was through renal vein (21.2%) followed closely by pelvicalyceal system (19.1%) and capsular invasion (19.1%). In contrast, capsular invasion was the most common route of spread in studies by Latif et al[1], Hashmi et al[2] and Hartmann et al[5]. Furhman nuclear grade was

applied only to clear cell RCC and tumours were grouped from grade I to grade IV. Majority of our tumours were in Grade II (63.8%) and a similar trend was observed by Latif et al[1] and Hashmi et al[2].

Table 9: Grading of clear cell RCC: Furhman nuclear grade

Studies	Grade I	Grade II	Grade III	Grade IV
Latif et al[1] (N=40)	6.6%	63.3%	20%	10%
Amin et al[6](N=377)	6%	21.6%	53.2%	19.6%
Hashmi et al[2](N=50)	---	71%	25.8%	3.2%
Present Study	16.6%	63.8%	13.8%	5.55%

The following table depicts TNM staging of our tumors with other studies.

Table 10: Staging of RCC

Studies	Stage I	Stage II	Stage III	Stage IV
Latif et al[1] (N=40)	31.7%	31.7%	36.7%	-------
Amin et al[6] (N=377)	51.4%	13.9%	22.6%	12.1%
Siddharth et al[3](N=50)	52%	32%	14%	2%
Present Study (N=47)	46.8%	8.5%	36.1%	8.5%

Fig. 1: Clear Cell RCC: Well circumscribed Tumour mass measuring 4 cm in diameter at midpole. on C/S variegated, yellowish white with focal areas of hemorrhage and necrosis

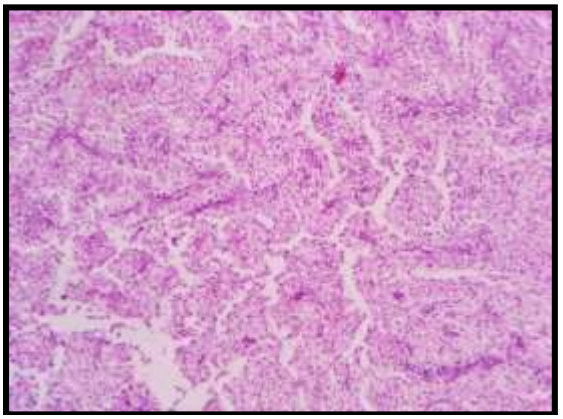

Fig. 3: Grade I Clear Cell RCC – showing cells with clear cytoplasm in solid, alveolar and acinar pattern. Nuclei resembling mature lymphocytes(H&E 100X)

Fig. 2: CLEAR CELL RCC :Well circumscribed tumour mass measuring 4x4x2 cm at the lowerpole of kidney. On C/S, solid yelowish white with areas of hemorrhage and necrosis

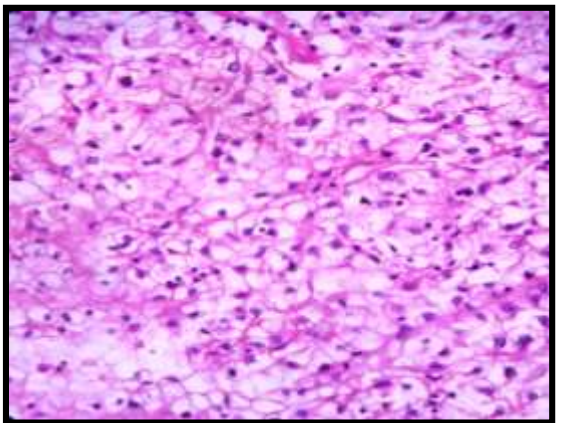

Fig. 4: Grade II Clear Cell RCC – clear cells with nuclei having open chromatin and inconspicuous nucleoli. (H&E 400X)

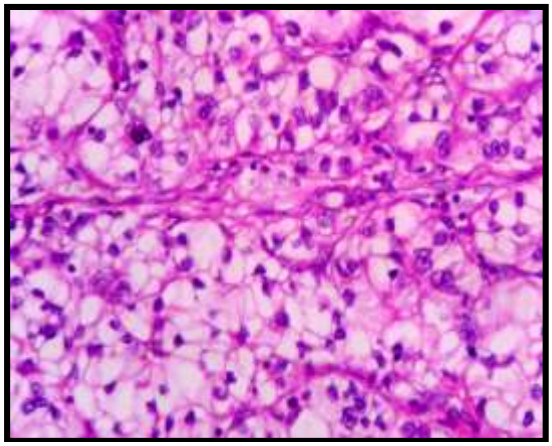

Fig. 5: Grade III Clear Cell RCC – nuclei showing nucleoli and cells with pleomorphism. (H&E 400X)

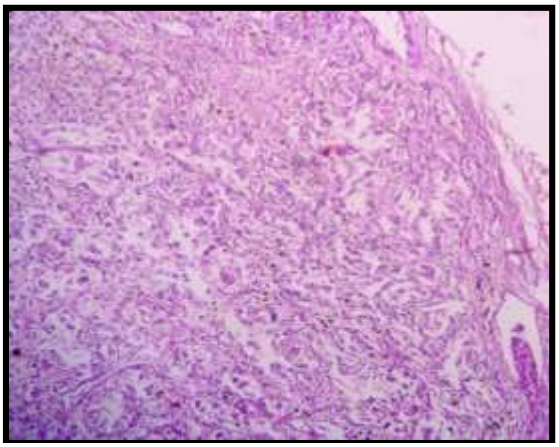

Fig. 6: Grade IV Clear Cell RCC – cells showing pleomorphism, hyperchromasiaand prominent nucleoli. (H&E 100X)

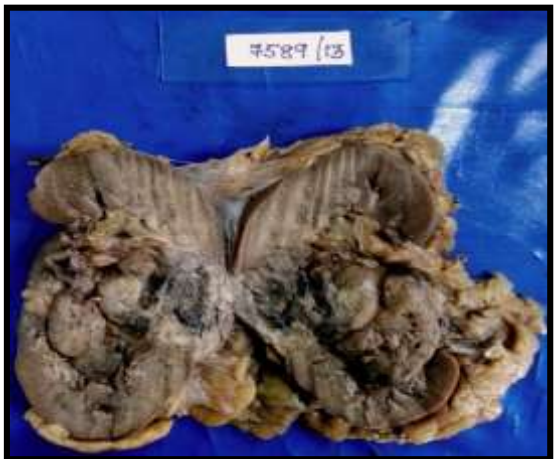

Fig. 7: Papillary RCC: Polypoidal mass in the mid pole of the kidney measuring 5x4.5x2cm extending into renal pelvis. On C/S, it is greyish white with areas of hemorrhage and necrosis

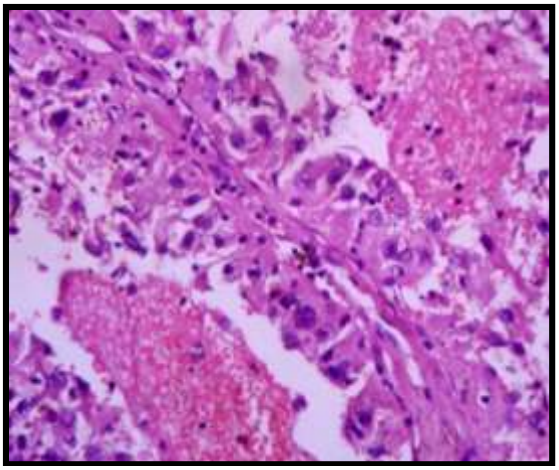

Fig. 8: Papillary RCC – type 2– Tumour cells showing nuclear pleomorphism, eosinophilic cytoplasm.(H&E)

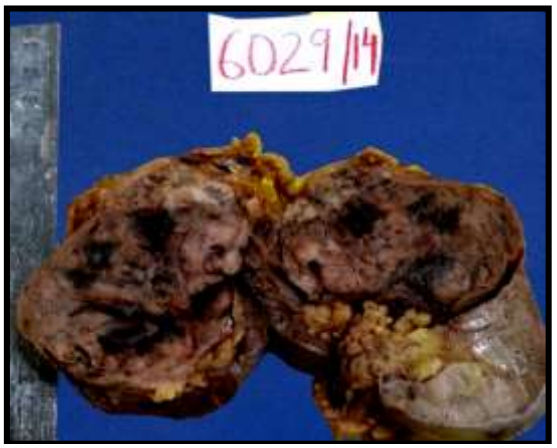

Fig. 9: Chromophobe RCC: 7x6x4 cm well circumscribed solid tumour involving upper half of the kidney. On C/S, brownish with areas of hemorrhage

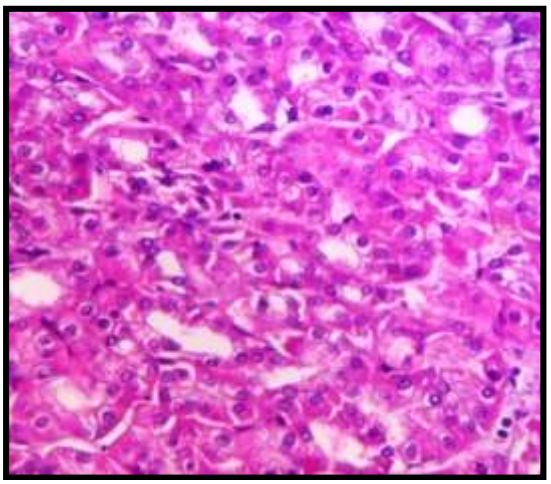

Fig. 10: Chromophobe RCC – polygonal cells with eosinophilic cytoplasm, irregular wrinkled nuclei and perinucleaar halo.(H&E 400X)

Fig. 11: Leiomyosarcoma of kidney: 10x8x8cm nodular mass involving the entire kidney. On C/S, whorled appearance is seen with focal areas of hemorrhage and necrosis

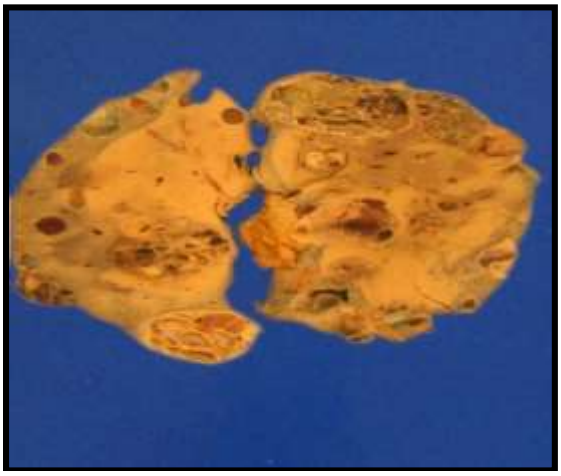

Fig. 12: VHL (Clear Cell RCC): Bilaterally enlarged kidneys measuring12x6x4cm

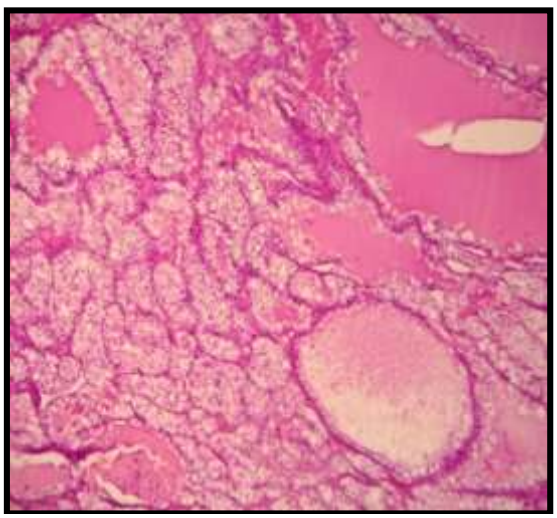

Fig. 13: VHL- Clear Cell RCC showing alveolar and microcystic and macrocystic pattern.(H&E 100X)

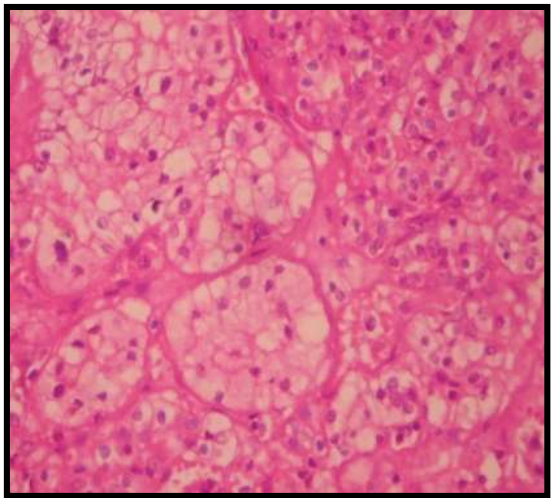

Fig. 14: Grade II Clear Cell RCC- cells with clear cytoplasm arranged in acinar pattern (H&E 400X)

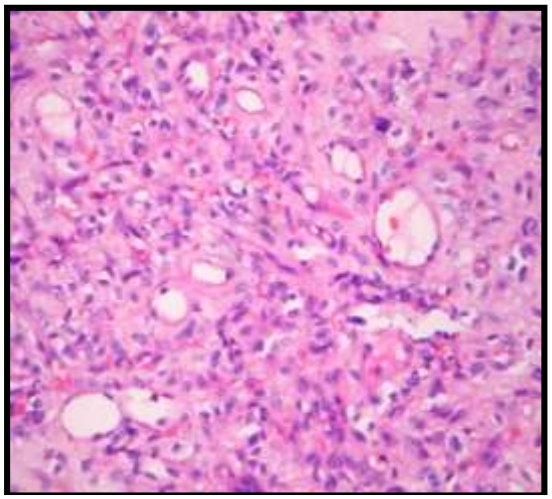

Fig. 15: Hemangioblstoma –clusters of stromal cells separated by multiple vascular channels (H&E 100X)

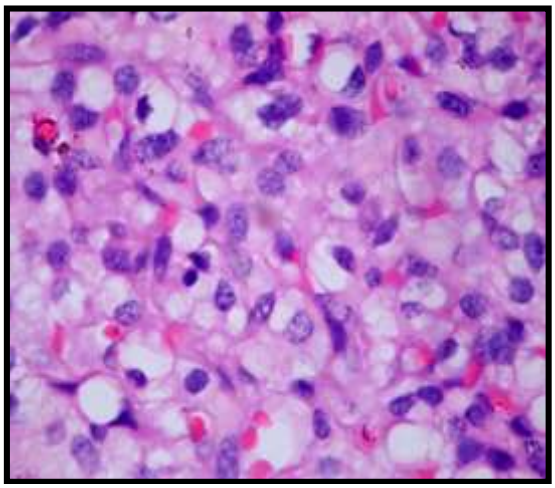

Fig. 16: Hemangioblastoma – Large polygonal cells with lipid laden cytoplasm and hyperchromatic nuclei. (H&E 400X)

Fig. 17: Angiomyolipoma: Tumour measuring 5x4x3 cm. On C/S, solid, yellowish white

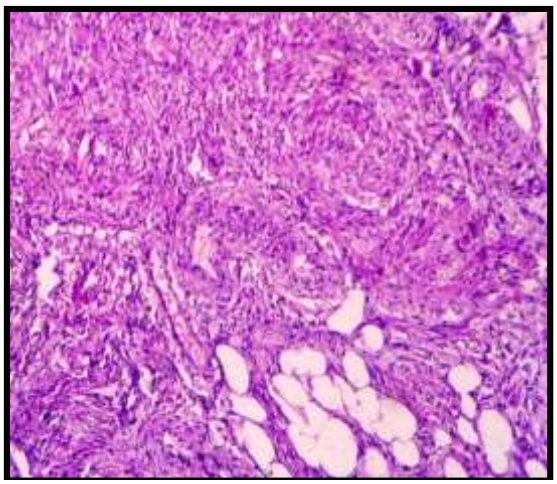

Fig. 18: Angiomyolipoma -Mixture of mature fat, thick-walled poorly organized blood vessels and smooth muscles

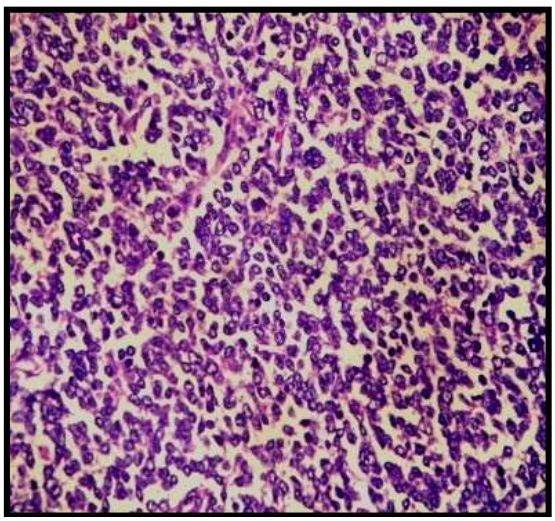

Fig. 19: PNET - monotonous polygonal cells with hyperchromatic round nucleus and micronucleolus. (H&E100X)

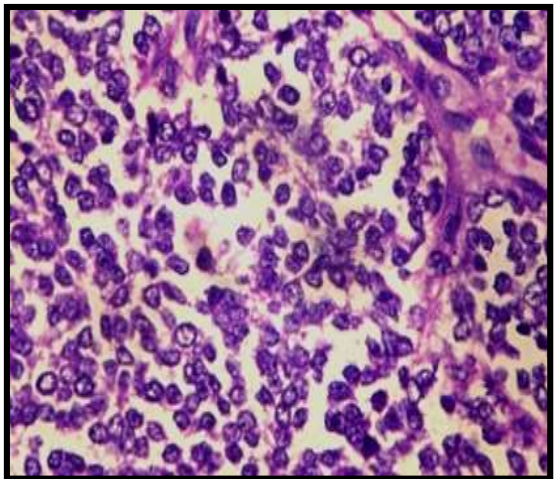

Fig. 20: PNET- Hyperchromatic nuclei with brisk mitotic activity. (H&E 400X)

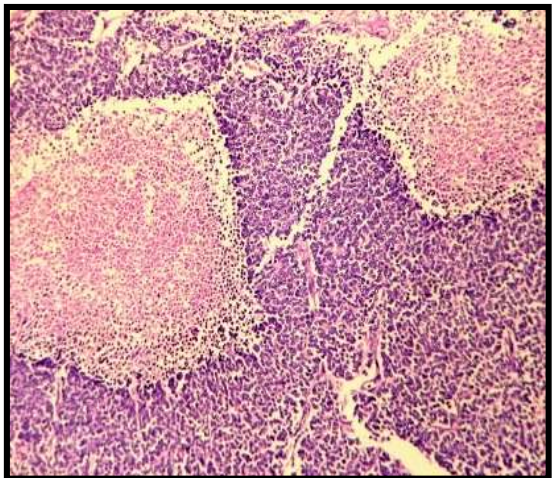

Fig. 21: PNET – tumour with extensive areas of coagulative necrosis. (H&E 100X)

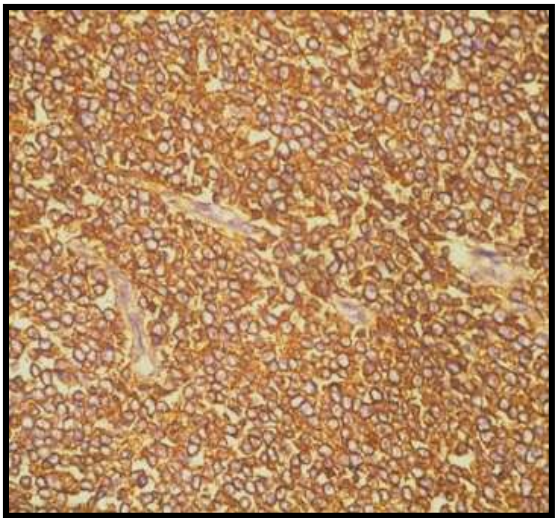

Fig. 22: PNET- Tumour cells showing CD99 positivity. (100X)

Angiomyolipoma

We observed 6 cases of angiomyolipoma in our study with a M:F ratio of 1: 5. The age ranged from 21 to 65 years with a mean age of 35 years. Majority of angiomyolipoma in our study involved the lower pole of the right kidney with a mean tumour size of 8.91cm. Graham et al[7] studied 11 cases of angiomyolipoma out of 149 tumours and found M:F ratio of 1:10. Another study conducted by Kulkarni et al[8] also showed a female preponderance with M:F ratio of 1:8.

We did not found any association with tuberous sclerosis in our study whereas Graham et al[7] encountered a single case associated with tuberous sclerosis.

Sarcomas

We observed only 2 cases of sarcoma in our study. One was in 60year old male with bosselated mass arising from renal pelvis. On cut surface it showed whorled appearance and histologically tumour showed features suggestive of low grade Leiomyosarcoma. Leiomyosarcoma may arise from the renal capsule, renal parenchyma, pelvic musculature or the main renal vein. Leiomyosarcomas of the kidney should be differentiated from the sarcomatoid variant of renal cell carcinomas, atypical angiomyolipomas, and genitourinary pacemaker cell tumours. Grignon et al[9] in their study suggested that to make a diagnosis of a primary renal sarcoma the following criteria should be met: 1) the patient must not have or have had a sarcoma elsewhere to rule out metastasis, 2) gross must be compatible with origin in the kidney rather than involvement due to retroperitoneal sarcoma 3) sarcomatoid renal cell carcinoma must be excluded. Second case detected in our study was in 19 year old female with a 25x13x12cm which on histology was composed of spindle cells arranged in herring bone pattern and thus was diagnosed as high grade sarcoma. Due to loss of follow up, Immunohistochemistry could not not be done in this case.

PNET

We observed a single case of PNET in our study in a 25 year old female. Latif et al[1] also encountered a single case of PNET in a 17 year old female in a study of 47 renal tumours. Pathological stage is the major determinant in the prognosis of PNET. Our case was in stage IV.

Metanephric Adenoma

We observed a single case of metanephric adenoma in our study. 30 year old male presented with painless hematuria. Schmelz etal[10] also reported a single case of metanephric ademoma in a 42 year old male with no physical complaints. Grossly, it was 3.8x4 cm mass.

Oncocytoma

Two cases of oncocytoma were detected in our study comprising 3.33% cases out of which one was incidentally detected tumours were solid, tan yellow with areas of hemorrhage with a mean size of 3.75 cm. Histologically, tumours were composed of oncocytes arranged in solid sheets and nests. Perez et al[11] studied 70 patients of oncocytoma in which 80% patients were asymptomatic whereas flank pain and abdominal mass was observed in 4% cases.

Renomedullary Interstitial Tumour (RMICT)

We observed a single case of renomedullary interstitial cell tumour in our study. 22 year old female who died of post-partum hemorrhage. The incidence of renomedullary interstitial cell tumour in autopsies has been reported to be 26 to 41%. These tumours are seen in both sexes with equal frequency and are not found in children. However there are few case reports of young patients too like our case.[12] Renomedullary interstitial cells exert an endocrine like antihypertensive effect[13]. There is an association with hypertension in many of the reported cases of renomedullary interstitial cell tumour. Our patient also had history of PIH and the heart at autopsy showed left ventricular hypertrophy.

Conclusion

The gold standard in the treatment of renal tumours is radical or partial nephrectomy. A detailed and meticulous histopathological examination of tumour nephrectomy specimen is essential to establish histological type and to evaluate histopathological prognostic determinants. The clinical outcomes of the various histologic subtypes are different. This further lends support to the morphologic and reported cytogenetic–molecular distinctiveness of the subtypes of renal epithelial neoplasms, further validating the contemporary classification scheme and underscoring the need for accurate subtyping of these tumours in clinical practice.

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