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HISTOPATHOLOGICAL STUDY OF TUMOURS AND TUMOUR LIKE LESIONS OF KIDNEY AND RENAL PELVIS

Pathology

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ABSTRACT

Background : Tumour and tumour like lesions of kidney and renal pelvis include a wide spectrum of entities. Renal neoplasms occurs both in adults and in children, with few rare tumours and account for 1% to 2% of all body cancers. Majority of which are RCC. Tumour and tumour like lesions of kidney and renal pelvis may present with nonspecific clinical manifestations, incidental findings on radiology or at autopsy, may present with the classical triad of flank pain, haematuria and abdominal mass or can be asymptomatic. Hence histopathological examination is essential for the diagnosis of renal neoplasms.

Material and method : It is retrospective study (July 2003 to June 2013) for a period of 10 years. Histopathological features of 38 tumours and tumour like lesions of the kidney and renal pelvis were analysed.Out of 38 cases, 27 were nephrectomy specimens and 11 were renal biopsies The histopathological reports and clinical details were collected and corresponding slides were reviewed. Tumours are classified according to WHO classification 2016.

Results: The present study included 38 cases of tumour and tumour like lesions of kidney and renal pelvis. Histopathological evaluation revealed malignant neoplasms in 27 (71.05%) cases, benign neoplasm in 5 (13.15%) cases and tumour like lesions in 6 (15.79%) cases.Among malignant tumours, clear cell RCC was the most frequent tumour in our study observed in 13 (86.67%) cases. Overall higher numbers of tumours and tumour-like lesions of kidney and renal pelvis were seen in the first decade of life followed by 4th to 5th decade of life in our study with a male predominance having M:F ratio of 1.23:1.

Conclusion: Malignant tumours outnumbered the benign tumours. Most of the malignant, benign and tumour like lesions present with similar clinical features hence histopathology remains the gold standard method.

KEYWORDS

Renal cell carcinoma, nephrectomy, Histopathology, nephroblastoma

INTRODUCTION :

Renal cell carcinoma is the 13th most common malignancy worldwide[1]. Renal neoplasms include a wide spectrum of entities both in adults and in children. The widespread use of abdominal ultrasonography and CT as investigative tools for many non-urological complaints led to a dramatic increase in the detection of small asymptomatic incidental renal masses. The incidence of benign renal tumours is low[2,4,5]. Benign tumours are renal adenoma, metanephric adenoma, renal oncocytoma, etc. Malignant epithelial neoplasms include clear cell variant of renal cell carcinoma (RCC), papillary RCC, chromophobe RCC, collecting duct RCC and the medullary carcinoma variant. The most common childhood tumour is nephroblastoma and the most common adulthood tumour is renal cell carcinoma. Amongst tumour like lesions xanthogranulomatous pyelonephritis, malakoplakia and renal cysts are the most common[3,4].

MATERIAL AND METHODS

The retrospective study was conducted in the Department of Pathology, Government Medical College, Miraj from June 2003 to July 2013. Total 38 cases were studied, out of which 25 were nephrectomy specimens and 11 were kidney biopsies and 2 kidney specimen were taken from autopsies studied. The nephrectomy specimens were fixed in 10% buffered formalin. After fixation specimen was measured, weighed and oriented. Gross photographs of the specimen were taken. Detailed gross examination of external surface, cortex, medulla, pelvis, ureter, renal artery and vein, perirenal lymph nodes was carried out. Stripping of the capsule was done to look for invasion. After the gross examination of the specimens, a minimum of four sections were taken from the tumour. Sections were taken from the pelvis, ureter, renal vessels, capsule and lymph nodes if present. Tumour particulars were noted with respect to size, surface, margins and extension. The tissue was processed as per the standard procedure 4-5 micron sections were cut on a microtome and stained by Haematoxylin and eosin stain. Microphotographs of the tumours were taken to represent different histological types of renal tumours. The histopathological reports and clinical details were collected. Corresponding slides were collected and reviewed for the confirmation of diagnosis. Tumours were classified according to WHO classification 2016.

RESULTS

In the current study, out of 38 cases, 27 (71.05%)were malignant neoplasms, 5 (13.15%) were benign neoplasm and 6 (15.79%) were tumour like lesions**(Table 1)**.

Table 1: Frequency of kidney and renal pelvis lesions

Type of lesion	Number of cases	Percentage
Benign tumours	05	13.15
Malignant tumours	27	71.05
Tumour like lesions	06	15.79
Total	38	100

Among malignant tumours, the most common primary malignant tumour of the kidney was renal cell carcinoma observed in 15 cases (39.47%), followed by nephroblastoma - 5 cases (13.15%) and single case of clear cell sarcoma and leiomyosarcoma each (2.63%). In epithelial tumours of the renal pelvis 4 cases (10.52%) of transitional cell carcinoma and a single case (2.63%) of mucinous adenocarcinoma were seen. Among the benign neoplasms, papillary adenoma - 2 (4.65%) cases, congenital mesoblastic nephroma - 2 cases (4.65%) and a single case of renomedullary interstitial tumour of the kidney (2.32%) were reported. In tumour like lesions, 6(15.78%) cases of xanthogranulomatous pyelonephritis were reported. **(Table 2)**

Table 2: Frequency of histological types of tumours and tumour like lesions of kidney and renal pelvis

Tumour like lesion		
	No. of cases	Percentage
1)Xanthogranulomatous pyelonephritis	6	15.78
Benign lesions		
	No.of cases	Percentage
1)Papillary Adenoma	2	5.26

2)Renomedullary interstitial tumour of Kidney	1	2.63
3)Congenital mesoblastic Nephroma	2	5.26
Malignant lesions		
	No. of cases	Percentage
1)Renal cell carcinoma	15	39.47
2)Nephroblastic tumours - Nephroblastoma	5	13.15
3)Mesenchymal tumours - Clear cell sarcoma - Leiomyosarcoma	1 1	2.63 2.63
4)Epithelial tumours of the renal pelvis - Transitional cell Ca - Adenocarcinoma	4 1	10.52 2.63
Total	**38**	100

Overall higher number of tumours and tumour like lesions of kidney and renal pelvis were seen in the first decade of life 10 cases (26.32%) followed by 4th to 5th decade of life 9 cases (23.68%) in our study showed a male predominance having M:F ratio of 1.23:1. **(Table.3, 4)**

Table 3: Age-wise distribution of tumours and tumour like lesions of kidney and renal pelvis

Age group	Cases	Percentage
0-10	10	26.32
11-20	1	2.63
21-30	2	5.26
31-40	0	0
41-50	9	23.68
51-60	8	21.05
61-70	6	15.79
71-80	2	5.26
Total	**38**	**100**

Table 4: Gender wise distribution of tumours and tumour like lesions of kidney and renal pelvis

Lesions	Males	Females
Tumour like lesions	5	1
Benign	2	3
Malignant	14	13
Total	**21**	**17**

Tumour and tumour like lesions of kidney and renal pelvis may present with nonspecific clinical manifestations, incidental findings at autopsy, may present with the classical triad or can be asymptomatic. In our study only 2 cases (5.26%) presented with classical triad. Ten cases (26.31%) showed asymptomatic manifestations and 3 (7.89%) were found incidentally at autopsy. **(Table 5)**

Table 5: Distribution of clinical features of tumour and tumour like lesions of kidney

Clinical features	No.of cases	Percentage
Lump in the abdomen(mass)	17	44.7
Flank pain	16	42.10
Haematuria	11	28.94
Classical triad(mass, flank pain, haematuria)	02	5.26
Non-specific symptoms(Weight loss, anorexia)	10	26.31
Asymptomatic(Incidental findings at autopsy)	03	7.89

The renal cell carcinoma constitutes 15 cases in this study. Clinically the main presenting symptoms of renal cell carcinoma were haematuria, flank pain and a lump in abdomen. Haematuria, was present in 3 cases (20%) while flank pain in 7 cases (46.66) and abdominal lump in 9 cases (60%). This classical triad is supposed to be diagnostic of renal cell carcinoma which was noted only in 2 (13.33%) cases **(Table 6)**.

Table 6: Distribution of clinical features of renal cell carcinoma

Clinical features	No.of cases	Percentage
Lump in the abdomen(mass)	09	60
Non-specific symptoms(Weight loss, anorexia)	08	53.33
Flank pain	07	46.66
Haematuria	03	20
Classical triad(mass, flank pain, haematuria)	02	13.33

Microscopically the renal cell carcinomas showed various cell types and histological patterns according to which they were segregated. Clear cell RCC was reported in 13 cases (86.67%). Papillary and unclassified RCC was seen in one case (6.66%) each. **(Table 7)**

Table 7. Distribution of various types of renal cell carcinoma

Type of RCC	No. of cases	Percentage
Clear cell RCC	13	86.67
Papillary RCC	1	6.67
Unclassified RCC	1	6.67
Total	**15**	**100**

There were 5 cases of nephroblastic tumours in this study. Clinically the patients with Wilms tumour presented with abdominal mass, abdominal pain and haematuria. The relative frequency of these symptoms is shown in **(Table 7).** Majority of cases (60%) presented with a lump in the abdomen and flank pain. Haematuria was observed in 1 case (20%).

Table 8: Distribution of clinical features of Wilms tumour

Clinical features	No of cases	Percentage
Abdominal mass	3	60
Flank pain	3	60
Haematuria	1	20

There were 5 cases of malignant tumours of the renal pelvis. Clinically the patients presented with haematuria, flank pain and abdominal mass. Haematuria was the most common symptom (80%) followed by flank pain 66.66%) and palpable mass (66.66%). **(Table 9)**

Table 9: Distribution of clinical features of renal pelvic tumour

Clinical manifestation	No of cases	Percentage
Gross haematuria	4	80%
Flank pain	3	66.66%
Palpable mass	3	66.66%

Tumour like lesions constituted 6 cases of Xanthogranulomatous pyelonephritis.

Majority of the patients presented with flank pain (66.66%), followed by fever (50%), palpable mass (33.33%) and urinary tract infection. **(Table 10)**

Table 10: Distribution of clinical features of Xanthogranulomatous pyelonephritis

Clinical manifestation	No of cases	Percentage
Flank pain	4	66.66%%
Fever	3	50%
Palpable mass	2	33.33%
Haematuria	2	33.33%
Dysuria	2	33.33%

DISCUSSION

We have attempted to evaluate the histopathological spectrum of tumour and tumour like lesions of the kidney and renal pelvis according to WHO 2016.

The most common malignancy encountered in our study is renal cell carcinoma (RCC) (39.47%) with the most common variant being clear cell type. The majority of the cases occurred in 6th to the 7th decade of life and showed an M:F ratio of 1.5:1.A lump in the abdomen was noted in the majority (60%) of the cases of renal carcinoma in our study. Papillary and unclassified RCC was seen in one case each. The frequency of renal cell carcinoma in the present study is similar to the study reported by Suvvari J et al[4] and Basavaraj Y et al[2]

Clear cell renal cell carcinoma is known to originate from the renal tubular epithelium. The clear cytoplasm is due to the presence of intracytoplasmic glycogen and lipid[5]. In the present study 13 cases of clear cell RCC accounted for 86.67%. Sarcomatoid changes occur in about 5% of the tumours and are associated with worse prognosis[5].Sarcomatoid change was seen in two cases in our study. Amongst 13 cases, six were nephrectomy specimens and five were biopsy specimens. Grossly, most of the tumour showed a bosselated external surface, thickened capsule which could not be stripped off

easily. Biopsy specimens showed yellowish to grey-white tissue measuring 0.5 to 2cm in largest diameter. Microscopy showed cells with clear cytoplasm arranged in nests, sheets, glandular and pseudoglandular pattern surrounded by intricately branching vascular septae. **(Figure 1)**. The frequency of clear cell RCC in the present study is similar to the studies done by Basavaraj Y et al[2] and Aiman A et al[4].

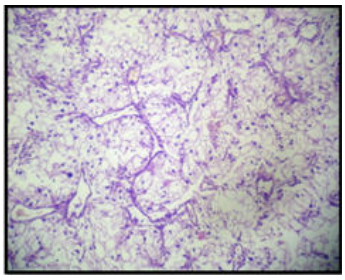


Figure 1. Clear cell RCC showing solid nests of clear cells surrounded by intricately branching vascular septae (x4, H&E)

Papillary renal cell carcinoma is the second most common variant of renal cell carcinoma[2,4,6]. We found one case (6.66%) of a papillary variant of RCC. A nephrectomy specimen was received. Grossly kidney appeared distorted and showed bosselated appearance. Microscopy revealed a predominant papillary pattern. The papillae were lined by cuboidal to columnar cells having pleomorphic vesicular nuclei, prominent nucleoli and abundant eosinophilic cytoplasm. The core of papillae showed foamy macrophages.**(Figure 2**). Similar frequency and histopathological findings were reported by Basavraj et al[2] and Bashir N et al[6].

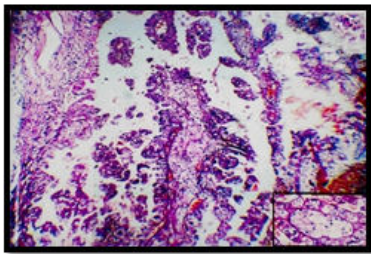
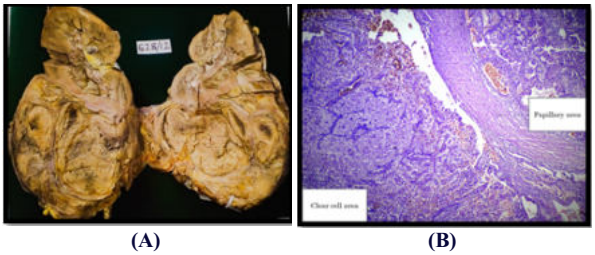


Figure 2.Papillary RCC showing papillary fronds with fibrovascular cores. Inset – foamy macrophages within the core (x10, H&E)

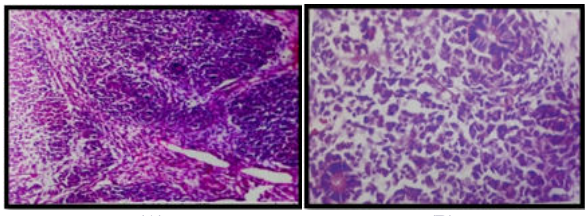
According to WHO 2016, unclassified RCCs have histological features that do not resemble those of any of the well-characterised RCC subtypes[5,6]. Features that place renal carcinoma in this category include apparent composites of recognised types, tumours with pure sarcomatoid morphology and no recognisable epithelial component, mucin production, mixtures of epithelial and stromal elements and unrecognisable cell types[7]. It is an aggressive form of RCC[8]. In our study, only one case (6.66%**)** of unclassified RCC was reported. A 60-year-old male presented with pain in the abdomen and haematuria. We received a nephrectomy specimen. Grossly, the tumour was large, grey-white to yellow and extensively involved the lower pole and middle portion of the kidney **Fig.3 (A)**. The tumour microscopically showed combined morphology showing clear cells and papillary architecture as shown in **Fig.3 (B)** The histopathological features are comparable with a case reported by Chander B et al[7].



(A) (B)

Fig 3. A) Gross photograph of unclassified RCC showing irregular infiltrative grey-white tumour with yellowish areas B) Microphotograph of unclassified RCC showing areas of papillary as well as clear cell RCC separated by fibrous band. (x4, H&E)

Wilms a tumour (Nephroblastoma**)** is the most common neoplasm of childhood accounting for more than 80% of renal childhood tumours[5,9,10]. Persistent islands of embryonal cells known as nephrogenic rest are believed to be precursor lesion[5]. Abdominal mass, abdominal pain, haematuria are common symptoms. In our study, there were 5 cases (24.24%) with a mean age of 2.5 years. Out of these, 3(60%) cases were between 2-3years of age with a male predominance. Abdominal mass and flank pain were noted in 60% of the cases in the present study. Four nephrectomies and a single biopsy specimen were received. Grossly, kidneys were enlarged, cut surface showed a prominent pseudo capsule enclosing solid, soft to firm, grey-white to grey tan mass. Microscopically all showed all the three histological cell types in varying proportion of blastemal, epithelial and stromal components. Blastemal component consisted of densely packed small round to oval cells with a scant amount of cytoplasm arranged in sheets. The epithelial component was characterised by the formation of embryonic tubular structures. The mesenchymal element had spindle cell fibroblast-like differentiation, particularly smooth muscle and skeletal muscle. **Fig.4 (A) & (B)**



(A) (B)

Figure 4. Wilm's Tumour showing predominant blastemal component A) With extensive necrosis B) With tubules and rosettes like structure. (x4, H&E)

The frequency of nephroblastoma in the present study correlated with the frequency reported by Basavraj et al[2], Mannan R[10] and Madhu Kumar R et al[11]

Clear cell sarcoma is a rare neoplasm of childhood[5]. Several authors including Marsden and his co-workers named it "Bone metastasizing renal tumour"[12]. The usual presentation is a child with flank mass with or without haematuria or sometimes present with pathological fracture due to metastatic tumour[13].

In this study, there was a case of clear cell sarcoma of the kidney in a $1^{1}/2$ year-old male who presented with abdominal mass and flank pain. The nephrectomy specimen grossly showed a friable grey white tumour. Extensive areas of necrosis and haemorrhage were noted. Microscopy revealed a tumour composed of small round to oval clear cells with vesicular nuclei, irregular nuclear membrane and inconspicuous nucleoli arranged in sheets and separated by delicate fibrous septae. A prominent arborizing vascular pattern was noted **(Fig. 5)** The histopathological and clinical findings are comparable with a case report by Gurusamy V et al[13]

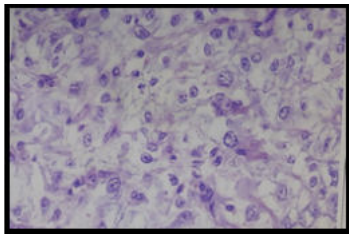


Figure 5. Clear cell sarcoma showing pleomorphic cells with clear cytoplasm, large nuclei with prominent nucleoli. (H&E,x40).

Primary Leiomyosarcoma(LMS) of the kidney is a rare tumour with aggressive behaviour[14]. LMS of the kidney was first described by Berry in 1919 but to date, these have been reported only as case reports or as a component of larger series of renal sarcoma literature. Histogenesis of renal LMS is believed to be from a renal capsule or smooth muscle fibres in the renal pelvis or from the renal vessels[15]. Most occur in adults with clinical symptoms of abdominal pain and haematuria. We reported a single case of leiomyosarcoma in a 25-year female who presented with abdominal mass. A renal biopsy specimen was received measuring 1cm in length. Microscopy showed alternating fascicles of pleomorphic, oval to spindle-shaped cells with elongated, blunt-ended

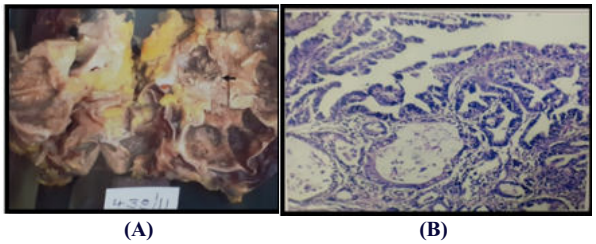
nuclei and a scant amount of eosinophilic cytoplasm. Few mitotic figures and areas of necrosis were seen. The final diagnosis given was suggestive of leiomyosarcoma. The immunohistochemistry was advised for final diagnosis. The microscopic findings, gender preponderance of a case reported in our study is comparable with a case report of Kusuma V et al[14] and Malik A et al[15].

Tumours of the renal pelvis comprise not more than 7% of those of renal parenchyma[16]. Approximately 90% of the tumours of the renal pelvis are transitional cell carcinoma[17,18].

The tumour is common in the 5th to 7th decade of life with male preponderance[10,17]. The common presentation is haematuria, flank pain and a palpable mass. Risk factors include advanced age, smoking, exposure to toxic industrial compounds[16] etc.

In our study, out of 5 cases of transitional cell carcinoma, in 3 cases nephrectomy specimen while in 2 cases biopsies of kidney were received. Haematuria was noted in about 80% of the cases reported. Grossly, kidneys were enlarged with thickened capsule and bosselated external surface. Microscopy showed round to polygonal cells with pleomorphic, hyperchromatic or vesicular nuclei and prominent nucleoli and a scant amount of eosinophilic cytoplasm arranged in multi-layered sheets, clusters, papillary and solid patterns. A single case was reported by Mannan R et al[10]and Bansal et al[17] in their study with similar findings.

Mucinous adenocarcinoma of the pelvis is an extremely rare tumour[18]. So far, approximately 100 cases have been reported in the literature. Most reported cases were commonly presented with haematuria and were identified in patients older than 60 years with no sex preponderance[19]. It usually occurs following glandular metaplasia of transitional epithelium induced by long-standing chronic inflammation, sometimes secondary to stones[19].In this study there was a single case of mucinous adenocarcinoma of the pelvis of 50 year-old female presented with abdominal pain in the left lumbar region. Nephrectomy specimen was received. Grossly kidney was enlarged, bosselated. The cut surface showed dilated pelvicalyceal system and revealed haemorrhagic mucoid material and multiple stones. **Fig. 6 (A).**Microscopy showed a tumour composed of round to oval cells with pleomorphic hyperchromatic to vesicular nuclei, prominent nucleoli and a moderate amount of eosinophilic cytoplasm arranged predominantly in tubulovillous and occasionally in the papillary pattern. Some of the tubules showed mucin in the lumina. **Fig 6 (B).** Similar clinical and histopathological findings were reported by Patel KN et al[18] and Raphael V et al[19]



(A) **(B)**

Figure 6. A) Gross photograph of mucinous adenocarcinoma of the renal pelvis. The pelvic cavity showed a polypoidal mass with papillary excrescences.

B) Photomicroghaph of mucinous adenocarcinoma showing glands and tubules lined by malignant intestinal-type epithelium with mucin in the lumina. (H&E,x40)

In 1967. Boland et al described CMN as a separate entity from congenital Wilms tumour and it is now considered as benign tumour[5]. It is low-grade fibroblastic neoplasm of the infantile renal sinus[17]. They are subclassified into classic and cellular. In our study, there were 2 cases (4.65%) with age less than 1 year. Out of these, one is a classic type and the other is a cellular type. Both were nephrectomy specimens. In classic CMN grossly kidney was well-circumscribed, solid, yellow-grey to tan with whorled configuration[5]. Microscopy revealed interlacing fascicles of fibroblastic cells with thin, tapered nuclei, pink cytoplasm, low mitotic activity and abundant collagen deposition. (**Fig. 7**). In **c**ellular CMN, grossly tumour had pushing borders and microscopy showed a tumour composed of poorly formed fascicles with sheet-like growth pattern.

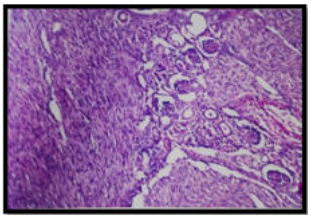


Figure 7.Congenital mesoblastic Nephroma showing fascicles of fibroblastic cells and normal renal parenchyma entrapped within the tumour.(x4,H&E)

The frequency of this tumour in the present study is 6.06% and is close to that reported by Reddy KR et al[20].

Papillary adenomas are tumours with papillary or tubular architecture and a diameter less than 15 mm[5]. It is usually an incidental finding at autopsy[21]. It is common in the population over the age of 65 years[21]. They arise in the renal cortex. In our study, we reported two cases as an incidental finding at autopsy. One was 55 years old male and the second was a 78year male. Gross examination of the kidney showed two tiny subcapsular yellowish nodules in one case and a single nodule with similar morphology in the other. Microscopic examination in both cases showed a well-circumscribed tumour composed of densely packed tubules and papillae lined by small cuboidal to columnar cells with uniform rounded nuclei. **(Fig 8).** The study was done by Basavaraj et al[2] and Chandanwale SS et al[22]shows comparable findings with the present study. The differential diagnosis for renal papillary adenoma is papillary RCC and metastatic papillary carcinoma.

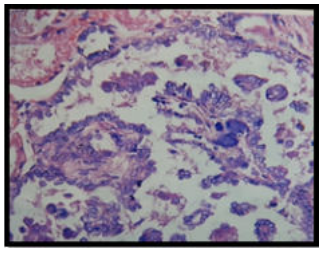
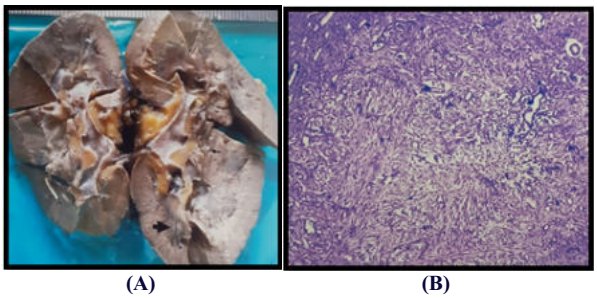


Figure 8.Papillary adenoma with the papillary architecture of cells around the fibrovascular core (x10, H&E)

Renomedullary interstitial tumours rare benign tumour of the renal medulla[23]. These are often found incidentally at autopsies and are asymptomatic[23,24]. Here we reported a single case as an incidental finding in an autopsy case of 20 year female with a history of fever and irrelevant talk. The clinical diagnosis was puerperal sepsis. Grossly, the kidney showed small whitish or pale-grey nodules on the cut surface. . **Fig.9 (A**).Microscopy revealed fairly circumscribed mass composed predominantly of spindle cells with bland oval nuclei arranged in intersecting bundles and short fascicles embedded in the loose vascular stroma. Normal renal tubules were entrapped, particularly at the periphery of the lesion. The differential diagnosis of this tumour should be distinguished from metanephric stromal tumour, mixed epithelial and stromal tumour. **Fig.9 (B**). Similar findings were reported in a case report of Agras K et al[24]



(A) **(B)**

Figure 9-A) Gross photograph of the cut surface of Renom edullary interstitial tumour showing small pale grey nodules. B) Microscopic photograph of Renomedullary interstitial tumour showing small spindled cells in faintly basophilic stroma (x4, H&E).

Xanthogranulomatous pyelonephritis(XPN) is a rare form of chronic

pyelonephritis, which is frequently associated with urinary tract obstruction, nephrolithiasis and concomitant infection with E-coli, proteus mirabilis, klebsiella, staphylococcus aureus etc[25]. The majority of the cases of XPN occurred in 6th to 7th decade of life with female preponderance[5].Preoperatively it may mimic renal tuberculosis or renal carcinoma due to nonspecific symptoms like fever, flank pain, weight loss, malaise[25,26]. In our study, A total of six cases of XPN were reported. From a total of 6 cases, all were nephrectomy specimens. Grossly two cases of the kidney showed thickened adherent capsule and cut the surface showed dilated pelvicalyceal system containing staghorn calculi. In the rest four cases, the corticomedullary junction was not identified and showed dilated pelvicalyceal system. Microscopy in all the cases revealed diffuse granulomatous inflammatory infiltrate composed of foamy histiocytes admixed with lymphocytes and plasma cells**. (Fig.10).** The findings of our study are comparable with Kundu R et al[26].

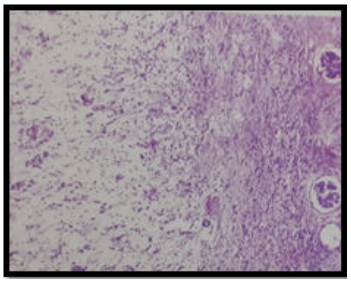


Figure 10. Microscopy of Xanthogranulomatous pyelonephritis showing abundant foamy histiocytes (x10, H&E)

CONCLUSION

Malignant tumours outnumbered benign tumours. Various benign lesions encountered were papillary adenoma, renomedullary interstitial tumour of the kidney and congenital mesoblastic nephroma. Renal cell carcinoma ranked high among malignant tumours. Out of which conventional/clear cell RCC was the most frequent histologic type affecting the age group with a peak during the 4th to 5th decade of life with a slight male preponderance. All malignant, benign as well as tumour like lesions present with similar clinical features hence histopathology remains the gold standard method.

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