International Journal of Current Research and Review
DOI: http://dx.doi.org/10.31782/IJCRR.2022.14910

Case Report

IJCRR
Section: Healthcare
ISI Impact Factor (2021-22): 2.176
IC Value (2020): 91.47
SJIF (2020) = 7.893

Compilation of Developmental and Neoplastic Entities in Kidney with Histomorphology and Immunohistochemistry as an Eye Opener in Troubleshooting the Diagnostic Errors

Das Saptangshu[1], Sneha[2], Ghosh Sukanya[3], Das Tushar Kanti[4]

[1]Junior Resident (Pathology), Department of Pathology, R G Kar Medical College & Hospital, Kolkata, India; [2]Senior Resident (MD Pathology), Department of Pathology, R G Kar Medical College & Hospital, Kolkata, India; [3]Senior Resident(MD Pathology), Department of Pathology, R G Kar Medical College & Hospital, Kolkata, India; [4]Professor and Head, Department of Pathology, R G Kar Medical College & Hospital, Kolkata, India.

ABSTRACT

Introduction: Renal cell tumours are common neoplasms with varying incidence and mortality rates across the globe. There are many histological types forming not merely the basis of classification but being associated with unique immunological and molecular profiles governing the biological behaviour. Apart from these, there are separate spectrum of neoplasms restricted particularly to paediatric age group. The overall prognosis is conferred by an array of factors including the histological grade, stage, necrosis and lympho-vascular invasion.

Case Reports: This discussion aims to outline the renal mass encountered in our setting with special reference to age group and the light microscopic picture. However, we encountered diagnostic dilemmas while dealing with the cases and these were further resolved employing relevant immunohistochemical markers. A particular mention of protocols for staging, grading and relevance of special stains has also been outlined.

Conclusion: To conclude, 1 case each of chromophobic renal cell carcinoma and infiltrating urothelial carcinoma of pelvis in middle aged adults have been discussed. 2 cases in paediatric age group have been highlighted namely triphasic nephroblastoma and multicystic dysplastic kidney (MCDK).

Key Words: Chromophobic, MCDK, Nephroblastoma, Renal cell carcinoma (RCC), Urothelial carcinoma, Wilms tumour

INTRODUCTION

Renal cell carcinoma includes heterogeneous neoplasms derived from renal epithelium and include diverse histological and molecular subtypes. Overall accounts for about 2 % cancer related mortality with highest incidence rates in developed country.[1] Clear cell RCC frequently associated with VHL mutation forms the most common subtype. This is followed by papillary[2] and chromophobic subtypes.[3] However a group of cases not fulfilling the criteria for any subtype are clustered under the common umbrella of unclassified RCC.[4] Localized RCC can be managed with nephrectomy while the metastatic ones often show resistance to conventional chemotherapy implicating the necessity to decipher the intratumoral heterogeneity which could be potentially targeted to significantly alter the outcome.

Nephroblastoma or wilms tumour (WT), the most common genito-urinary malignancy in children with a peak incidence between 2-3 years of age is known to be derived from nephrogenic blastemal cells.[5] This tumor shows divergent patterns of differentiation ranging from undifferentiated blastemal cells to differentiating epithelial (tubules) and stromal elements (skeletal muscle). Bilateral WT has syndromic association (WAGR, Denys-Drash and Beckwith-Wiedemann) and often shows multifocality and recurrence.[6] The International Society of Paediatric Oncology (SIOP) advocates preoperative therapy followed by surgical removal allowing for reduction in tumour burden and hence minimising the risk of intraoperative ruptures and more favourable stage distribution. Another widely used protocol, Children's

Corresponding Author:
Dr. Sneha, BD-075, First floor, Salt Lake, Sector-1, Kolkata, 700064, West Bengal, India.
Email: snehajha1492@gmail.com

ISSN: 2231-2196 (Print) **ISSN:** 0975-5241 (Online)

Received: 13.03.2022 **Revised:** 02.04.2022 **Accepted:** 18.04.2022 **Published:** 03.05.2022

Oncology Group (COG) however recommends the primary resection to be followed by therapy on the basis of primary biological parameters.

Multicystic dysplastic kidney, a congenital anomaly of urinary tract having multiple non-communicating cysts of varying sizes separated by primitive ducts, dysplastic renal parenchyma, lobar disorganization and metaplastic kidney.[7,8] The tubules lined by undifferentiated cells often mimic the blastemal rosettes of WT. The vesico-ureteric reflux and ureteropelvic junction obstruction leads to chronic pyelonephritis like picture morphologically rendering diagnostic difficulty.

This discussion deals with a set of 4 cases presenting as an abdominal mass, subjected to nephrectomy and histopathological examination. The salient pointers for diagnosis and excluding the mimickers has been put forward.

CASE SERIES

(1) 35-years-old female, presented with an abdominal mass. On imaging, a lobulated heterogeneously enhancing 10x8 cm mass situated in the left kidney with no extension into surrounding tissues or thrombus in renal vein or IVC.Grossly a well circumscribed tumour arising from lower pole of kidney, tan on cut section. M/E revealed dyscohesive cells arranged in sheets incompletely divided by vascular septa. The smaller cells with binucleation, wrinkled nuclei, perinuclear haloes with granular eosinophilic cytoplasm in the centre palisaded by larger cells with distinct cell membranes and pale reticular cytoplasm at periphery. It was reported as stage II chromophobic RCC.

(2) 60-years-old female with intermittent hematuria and flank pain underwent imaging showing a mass within the renal pelvis along with hydronephrosis in the renal parenchyma proximal to the lesion. On gross examination following nephroureterectomy, solid whitish mass measuring 4.2x3 cm was noted in the renal pelvis along with dilated pelvicalyceal system. Microscopically tumour cells were arranged in irregular nests with nucleomegaly, high grade nuclear pleomorphism, prominent nucleoli and frequent mitotic figures infiltrating the peri-pelvic fat. A final diagnosis of high grade, stage III invasive urothelial carcinoma was given.

(3) 3-years-old male boy with abdominal mass was operated in pediatric urosurgery. On cut section of right kidney, a well circumscribed nodular tumour measuring 7x5x2 cm with pale grey appearance occupying almost the entire kidney was found. H & E examination revealed triphasic growth pattern comprising serpiginous cords of monomorphic blastemal cells, tubular rosettes along with smooth muscles bundles and fibroblasts, rendering a diagnosis of triphasic nephroblastoma, local stage II as per COG. No foci of anaplasia or nephrogenic rests were noted.(Fig 5 and 6)

4) 3-months-old male baby with hydronephrotic changes in left kidney was excised. Grossly multiple cysts of varying size compressing the normal parenchyma, along with dilated pelvicalyceal system and poor cortico-medullary differentiation was seen. Microscopically cysts lined by primitive epithelium with a fibromuscular collar, lobar disarray and foci of mature cartilage were seen, along with thyroidization of tubules and mononuclear cell infiltration in the interstitium. A final diagnosis of MCDK was made. (Fig 7)

DISCUSSION

Renal tumours, although sharing a common origin from renal cells represent distinct clinico-pathological entities. [9,10] The histomorphological picture characteristic in certain cases should not however be used as sole criteria for categorising into subtypes, as many cases with clear cell and papillary pattern may belong to other classes on extensive study applying molecular markers significantly altering the prognosis and hence taking this route stands clinically significant. We have presented 4 cases with distinct morphology in this context.

(1) The first case of this study includes a stage II chromophobic RCC in a 35 years old female. The characteristic finding in the case was peculiar morphology in the form of dual population of clear pale cells with plant cell like membranes and eosinophilic cells having raisinoid nuclei and koilocytic atypia. (Fig 1) On IHC CK7(membranous) and CD 117 (membranous) positivity were demonstrated. (Fig 2) Also, hale colloidal iron was diffusely cytoplasmic positive. However, the predominance of eosinophilic cells and well localisation of the tumour warranted the need to rule out hybrid oncocytic/chromophobic tumour which was proven by S100A negativity. The cytoplasmic eosinophilia made us look for Succinate dehydrogenase (SDHB) expression to avoid missing SDH deficient RCC which behave aggressively. Also, one needs to be cautious to look for minute areas of necrosis and sarcomatoid changes by extensive sampling which are independent prognostic factors in this neoplasm with an inherently low indolent behaviour. Also refraining from grading these by WHO/ ISUP grading system conventionally used for clear cell and papillary RCC is crucial as the nuclear characteristics inherently place them in higher grade category despite the good prognosis.

(2) The next case was stage III invasive urothelial carcinoma in a 60 years old female. In our case, the tumour was diffusely infiltrating the pelvic-calyceal system and the surrounding medullary renal parenchyma was free of tumor process. However, the high-grade nuclear morphology

made us skeptical to rule out other possibilities. A panel of IHC showed that the tumour was PAX 8, OCT 4 and INI negative eliminating collecting duct carcinoma, renal medullary carcinoma and type 2 papillary RCC. CK 7 positivity and nuclear expression of p63 strongly supported our diagnosis. (Fig 3) Hereditary leiomyomatosis associated RCC located to medulla with bizarre cells having prominent inclusion like eosinophilic nucleoli showing absence of fumarate hydratase (FH) staining and association with cutaneous and uterine leiomyomas is a rare possibility to be considered after ruling out others.

(3) A case of triphasic neuroblastoma in a 3 years old male child has been reported, which although is the most common pediatric neoplasm but often ruling out the other differentials of similar morphology especially in scenarios where one is dealing with biopsy from metastatic sites say retroperitoneal or abdominal tumours is essential. The blastemal component in association with tubular rosettes and stromal component further supplemented with nuclear WT immunoreactivity rendered the diagnosis straightforward. However, in case of blastemal predominant Wilms tumour (WT), peripheral neuroectodermal tumour(PNET) and Ewing sarcoma (ES), has to be ruled out by CD 99 staining. Also, teratoid WT with extensive heterologous differentiation has to be differentiated from immature teratoma with former showing histioid over the organoid pattern in the later. In cases having extensive epithelial differentiation, epithelial predominant nephrogenic rests and papillary RCC needs to be excluded. The stromal predominant morphology has to be distinguished from congenital mesoblastic nephroma which is most common in the first 3 months of life and has an indolent behaviour while WT demands chemotherapy. Also, clear cell sarcoma with pseudo-acinar patterns is a potential morphological mimicker in this age group but is medullary centred, has fine chromatin and hyalinised stroma and the final diagnosis needs demonstration of YWHAE-FAM22 gene fusion. Also, the coexistence of RCC although rare needs to be looked upon as in these cases both the entities need separate staging and the poorer stage decides the prognosis.
The significance of staging of WT has been mentioned already. The presence of focal or diffuse anaplasia and the presence of coexistent nephrogenic rests which increase the risk of contralateral nephroblastoma and needs chemotherapy to reduce the burden of nephroblastic tissue and restore the function of normal kidney parenchyma and salvage the tissue which would otherwise need surgical excision if transformed. Also, anaplastic tissue show resistance to adjuvant chemotherapy and they stand on post-chemotherapy and hence it is considered that the prognosis in these cases is decided by the completeness of surgical removal of such tissues. This however carries more relevance when considered along with pathological staging of the tumour. Also post therapy many of the elements show maturation particularly the striated muscle and the presence of these doesnot imply treatment failure however, response to therapy is assessed by necrosis which needs minimal treatment after surgery.

(4) A case of MCDK was reported in a 3 months old female. Grossly, presence of distorted pelvicalyceal system made us initially think along the lines of congenital hydronephrosis seen in association with urethral obstruction, fetal uropathy and vesico-ureteric reflux. [11] However, multiple cysts could not be still explained. The giant hydronephrosis may be associated with dysplasia, wherein dysplastic changes are seen in cortex and hydronephrotic features in medulla. In our case, the presence of an island of metaplastic mature cartilage representing the metanephric element in association with primitive ducts lined by undifferentiated epithelium and lobar disarray were very helpful clue for diagnosis of MCKD. However, the presence of mononuclear inflammatory cell, atrophic tubules with thyroidisation at places were a pointer for reflux. This was a very notable finding in our case as most of the cystic dysplastic kidneys are associated with pyelocalyceal occlusion, ureteral atresia and are not subjected to reflux. [12,13] This probably represent MCKD and congenital hydronephrosis to be a spectrum with few cases showing intermediate features as variants of obstructive dysplasia and congenital hydronephrosis. Autosomal recessive polycystic kidney disease (ARPKD) was ruled out in our case as it is associated with enlarged kidney, cortical edema, dilated sac like cysts arising from collecting ducts and tubules with normal lobar structure on histology. They are associated with congenital hepatic fibrosis leading to portal hypertension. On biopsy, enlarged portal areas with proliferating bile ducts forming anastomosing channels is seen. Also, MCKD may be associated with nodular blastema which can lead to WT and RCC. [14,15] However, no such foci were noted in this case. In the setting of well encapsulated cysts with clear demarcation from surrounding parenchyma and the cysts being separated by septa containing primitive blastemal elements the diagnosis of cystic partially differentiated nephroblastoma over cystic nephroma to be made where the primitive elements are lacking. Fig 4) Multilocular cystic RCC, rare event seen in the context of von Hippel-Lindau syndrome and cystic WT with presence of solid, expansile regions distorting the cyst spaces is another possibility.

CONCLUSION

RCC are diverse entities with varying morphology often diagnostic,limiting the use of IHC only in metastatic cases and in subclassification. However not all clear cell and pap-

illary morphology are proven to be clear cell and papillary RCC respectively. Here in comes the utility of molecular markers to rule out translocation and hereditary leiomyomatosis associated RCC. Birt-Hogg-Dube syndrome and SDHB associated RCC are other separate entities. In line with paediatric tumors elsewhere, these need special mention with respect to morphology and biology. Strikingly the developmental disorder particularly the cystic disorders often pose a diagnostic difficulty and apart from being risk factor could be coexistent with cystic RCC and WT, hence warranting the surgical excision and extensive examination. They also have syndromic association implicating multidisciplinary approach for management.

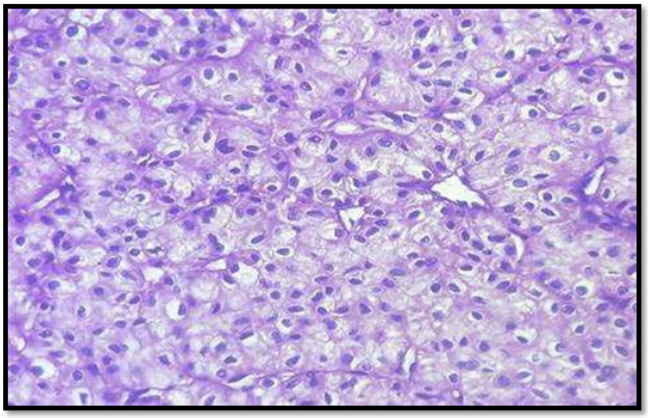

Figure 1: Chromophobic RCC, clear cells with koilocytic atypia.

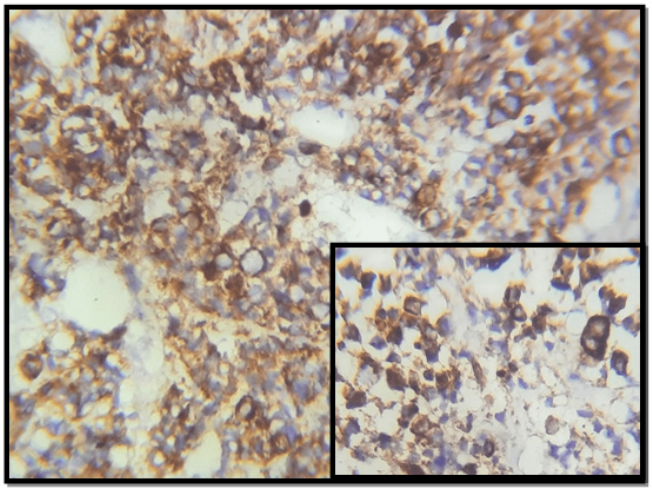

Figure 2: CK 7 immunostain, CD 117 in inset.

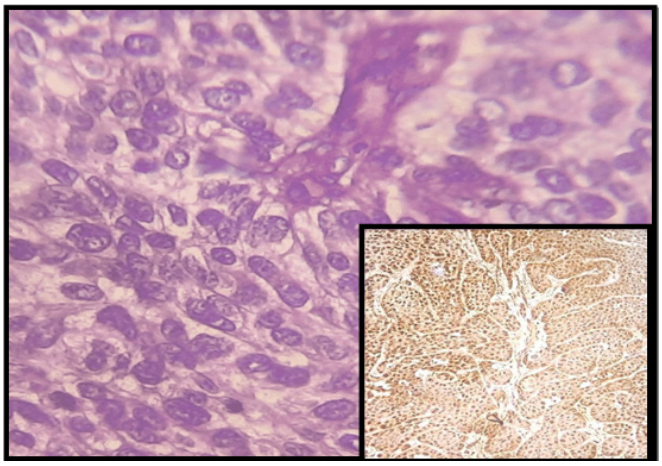

Figure 3: Invasive urothelial carcinoma, p63 immunostain in inset.

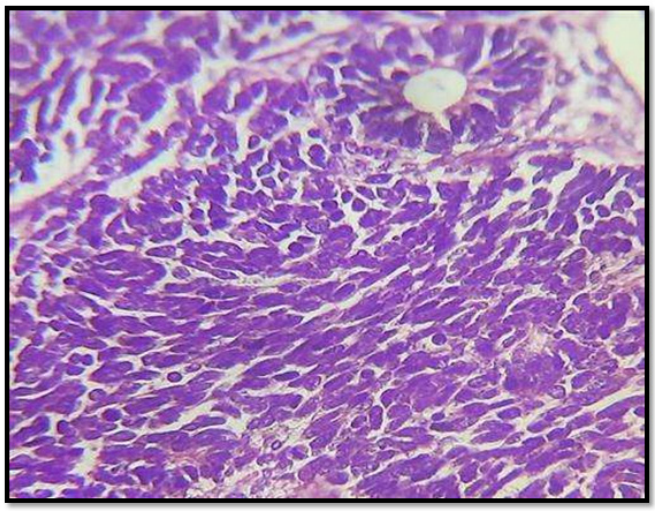

Figure 4: Blastemal elements.

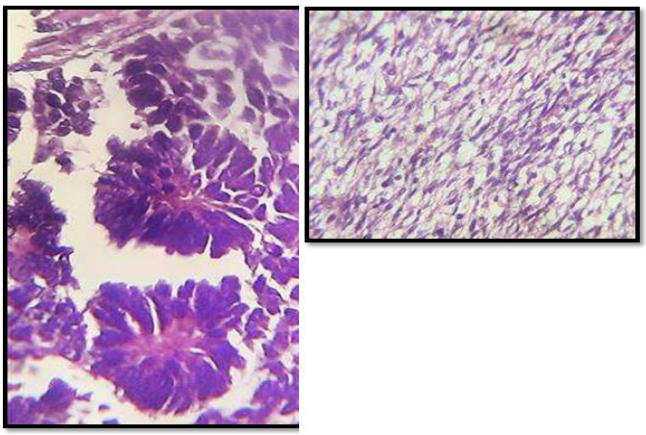

Figure 5: Tubular rosettes.

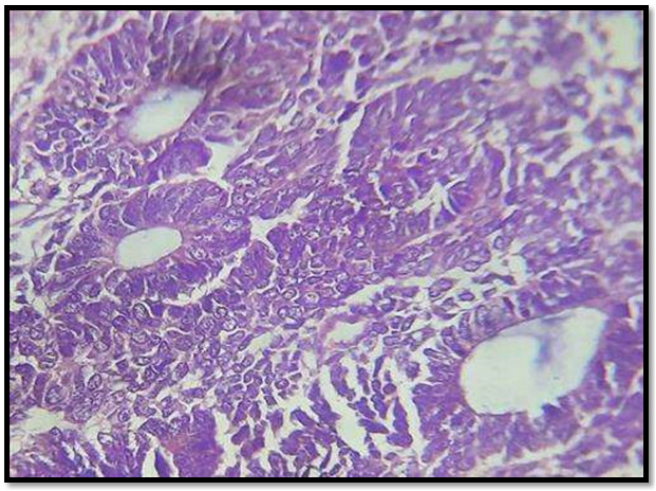

Figure 6: Heterologous glandular differentiation, smooth muscles in inset.

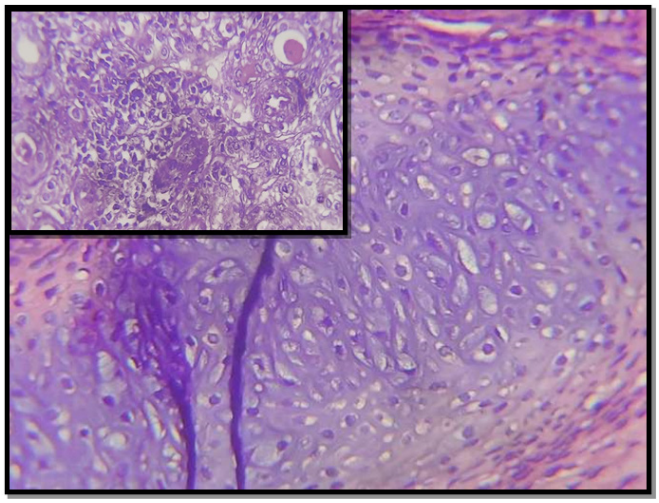

Figure 7: Cartilaginous foci, thyroidisation of tubules and mononuclear cells in inset.

ACKNOWLEDGEMENT

Authors acknowledge the enormous help from the scholars whose articles are cited and included in references of this manuscript. Also authors are highly grateful to the publications of the editors/ publishers from where the literature for this article has been taken, reviewed and discussed.

Conflict of Interest: None

Source of Funding: Self-funded

Authors' Contribution:

Dr Saptangshu Das - Framing of the concept behind the work, collection of data, review of literature and manuscript writing.

Dr Sneha- Corresponding and contributing author for manuscript writing.

Dr Sukanya Ghosh- Contributing author for manuscript writing.

Dr Tushar Kanti Das- Guidance and supervision, selection of the topic, necessary corrections and final shaping of this piece of work for submission.

REFERENCES

1. Ferlay J.GLOBOCAN 2012 v1. 0, Cancer incidence and mortality worldwide: IARC CancerBase No. 11. 2013.
2. Cancer Genome Atlas Research, N. Comprehensive Molecular Characterization of Papillary Renal-Cell carcinoma. NEJM. 2016; 374:135-145.
3. Davis CF. The somatic genomic landscape of chromophobic renal cell carcinoma. Cancer Cell. 2014;26:319-330.
4. Chen YB. Molecular analysis of aggressive renal cell carcinoma with unclassified histology reveals distinct subsets.
5. Denes FT, Duarte RJ, Cristofani LM. Pediatric genitourinary oncology. Front Pediatr. 2013;1:48. 10.3389/fped.2013.000048.
6. Romao RL, Pippi Salle JL, Shuman C. Nephron sparing surgery for unilateral Wilms tumor in children with predisposing syndromes: single center experience over 10 years. J Urol. 2012;188 (4 Suppl):1493-8. 10.1016/j.juro.2012.02.034.
7. Bernstein J. Developmental abnormalities of the renal parenchyma-hypoplasia and dysplasia. Pathol Annu 1968; 3:213-47
8. Bernstein J. The morphogenesis of renal parenchymal maldevelopment (renal dysplasia). Pediatr Clin North Am 1971; 18:395-407.
9. van den Berg E, van der Hout AH, Oosterhuis JW. Cytogenetic analysis of epithelial renal-cell tumors: relationship with a new histopathological classification. Int J Cancer 1993;55(2):223-227.
10. Weiss LM, Gelb AB, Medeiros LJ. Adult renal epithelial neoplasms. Am J Clin Pathol 1995;103(5):624-635.
11. Dudley JA, Hawarth JM, McGraw ME. Clinical relevance and implications of antenatal hydronephrosis. Arch Dis Child 1997;76:F31-F34.
12. Pathak IG, Williams DI. Multicystic and cystic dysplastic kidneys. Br J Urol 1963; 36:318-331.
13. Risdon RA. Renal dysplasia. I. A clinico-pathological study of 76 cases. II. A necropsy study of 41 cases. J Clin Pathol 1971;24:57-71.
14. Vellios F, Garrett RA. Congenital unilateral multicystic disease of the kidney. A clinical and anatomic study of seven cases. Am J Clin Pathol 1961;35:244-254.
15. Birken G, King D, Vane D. Renal cell carcinoma arising in a multicystic dysplastic kidney. J Pediatr Surg 1985;20:619-621.