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Histological Subtypes of Renal Cell Carcinoma- A Series of Case Reports.

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ABSTRACT

The kidneys are affected by various pathologies resulting in a spectrum of diseases, ranging from benign conditions to malignant pathology. Renal tumours encompasses a wide spectrum in all age groups. Renal cell carcinomas constitute majority of all renal neoplasms and are now exhibiting an increasing prevalence. Renal cell carcinoma represents a heterogenous disease with an ever increasing number of tumour subtypes. The World Health Organization classification, 2016, recognises the subtypes with Clear cell, Papillary and Chromophobe to be the most common of all the histological subtypes.

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INTRODUCTION

The kidney is one of the most highly differentiated organs in the body with a complex histologic structure as well as physiologic processes[1]. The kidneys are affected by various pathologies resulting in a spectrum of diseases, ranging from benign conditions to malignant pathology[2]. Renal tumours encompasses a wide spectrum in all age groups[3]. Renal cell carcinomas constitute majority of all renal neoplasms and are now exhibiting an increasing prevalence[4]. Renal cell carcinoma represents a heterogenous disease with an ever increasing number of tumour subtypes[5]. The World Health Organization classification, 2016, recognises the subtypes with Clear cell, Papillary and Chromophobe to be the most common of all the histological subtypes[6]. With an evolving classification, limited radiological contribution to accurate histopathological diagnosis, proper tumour typing is essential for a correct and methodic approach to disease management, thus, presenting a case series encountering the varied clinical details, histopathologic examination and patient approach to the various subtypes.

CASE PRESENTATION

CASE 1

A 54 year old male, came with history of bilateral hydrocele and left inguinal hernia since 2 weeks, which was confirmed on physical examination, along with an occasional history of haematuria. An ultrasonography was advised which incidentally found a 7.4 x 3.9 cm, heteroechoic mass lesion with few areas of hypoechogenicity indicating necrosis arising from the upper mid pole of right kidney. Few specs of calcification and loss of cortico-medullary differentiation was also noted. An impression of Renal Cell Carcinoma of right kidney was given. Further radiologic workup with CECT was advised which showed an exophytic growth extending into the pelvi- calyceal system. Right total nephrectomy was done and the specimen was sent for histopathological examination.

Gross Findings

Right radical nephrectomy specimen received measuring 20 x 10 x 8 cm with attached suprarenal gland and perirenal fat. Externally, the specimen was irregular, partially encapsulated with a bosselated appearance. Cut surface showed a well circumscribed, grey- yellow mass with a tan- yellow colour, solid and cystic appearance, areas of necrosis and haemorrhage along with complete distortion of the renal parenchyma. Sections were taken according to the grossing protocol and processed for microscopic examination.

Fig. 1: Cut surface of right radical nephrectomy specimen indicating a well circumscribed, grey- yellow mass with a tan-yellow colour, solid and cystic appearance along with areas of necrosis and haemorrhage. Complete distortion of renal architecture noted.

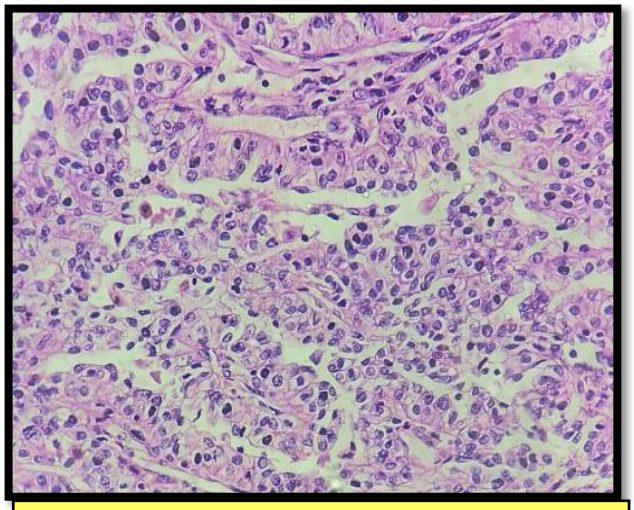

Fig. 2: H and E stained section, 10x. A papillary architecture emphasized by a delicate fibrovascular core lined by neoplastic cells is noted.

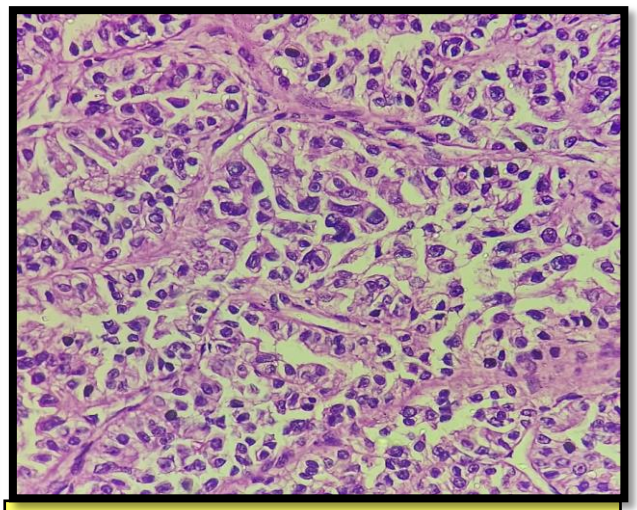

Fig 3: H and E stained section, 40x. The neoplastic cells of cuboidal to low columnar morphology, eosinophilic to amphophilic cytoplasm and pleomorphic nucleus exhibiting malignant features.

Microscopic examination: The features studied showed a circumscribed, pseudoencapsulated lesion with a predominantly papillary architecture emphasized by a delicate fibrovascular core lined by neoplastic cells of cuboidal to low columnar morphology, eosinophilic to amphophilic cytoplasm and pleomorphic nucleus exhibiting malignant features. Collection of foamy macrophages and few areas of necrosis and fibrosis was also noted. The final diagnosis was Papillary Renal Cell Carcinoma (Type II) with no lymphovascular, capsular and nodal invasion.

CASE 2

A 71 year old male, came with complaints of an abdominal lump in the left flank region since 2 years. The complaint was corroborated by examination and radiological investigation was advised in the form of CECT scan. Urine sample for malignant cell cytology was negative.

The imaging study revealed a large heterogeneously enhancing mass measuring 9.7 x 6.9 x 7. 5 cm occupying the left renal pelvis with adjacent upper and mid calyces showing multiple foci of intralesional calcification. The finding was suggestive of neoplastic pathology, likely to be Renal Cell Carcinoma.

Gross Features: Left radical nephrectomy specimen was examined, the findings noted were to be an enlarged, irregular specimen with an adherent capsule. Cut surface showed effacement of normal renal parenchyma. Two grey brown lesions were noted showing a lobular appearance with focal areas of haemorrhage and necrosis. Sections were taken for microscopic reporting.

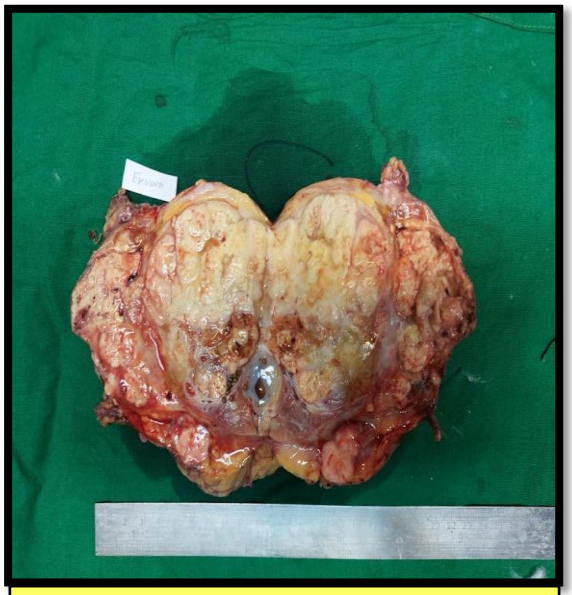

Fig. 4: Cut Surface of Left Radical Nephrectomy specimen.

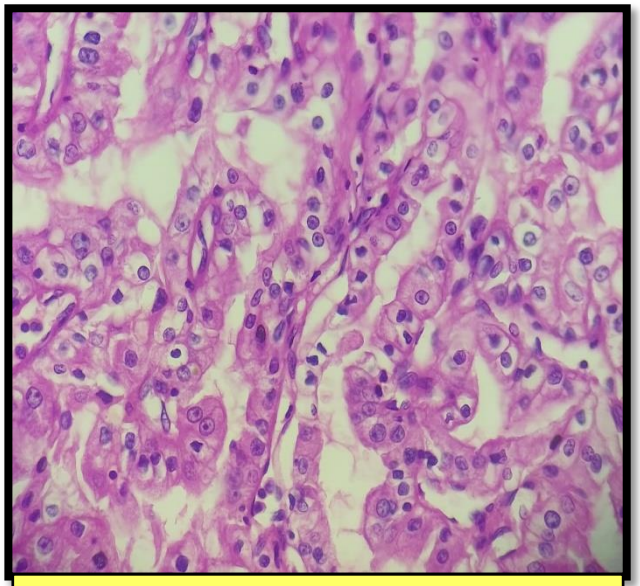

Fig. 5: H and E section, 40x. A trabecular pattern of neoplastic cells. Cells show distinct borders with raisinoid nucleus.

Microscopic findings: The haematoxylin and eosin stained sections showed neoplastic cells arranged in sheets and poorly formed trabecular pattern. The neoplastic cells composed of round to polygonal cells with distinct cell borders and pale staining abundant cytoplasm. The nuclei were irregular, wrinkled showing a raisinoid appearance with a perinuclear halo. Few cells were also noted to have a granular cytoplasm. Areas of necrosis and haemorrhage with focal areas of calcification was also noted. Chronic pyelonephritis was an additional pathologic finding. No nodes were

submitted to assess nodal involvement. The microscopic features were suggestive of Chromophobe Renal Cell Carcinoma.

CASE 3

A 68 year old male was referred to Urology OPD with complaints of pain in abdomen, insidious in onset since 1 year. Abdominal examination yielded no significant findings. Radiological investigations were advised.

The Ultrasonography as well as the CECT abdomen showed a large heterogeneously enhancing solid exophytic lesion arising from the lower pole of the right kidney and extending into the perinephric fat. Multiple, non enhancing necrotic areas were noted within the lesion. Patient was operated and specimen was sent for histopathology.

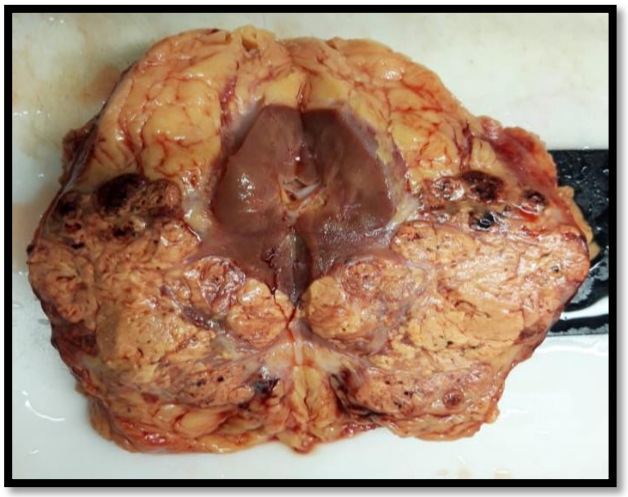

Fig. 6: Gross features of the specimen shows an irregular lesion with a variegated appearance.

Gross Features: The external surface was irregular, partially capsulated with focal areas of haemorrhage. Cut surface showed an exophytic lesion arising from the lower pole of kidney with a variegated appearance and focal areas of haemorrhage and necrosis. The tumour seemed to be in continuation with the lower pole of kidney. The cortico- medullary junction was distorted.

Microscopic features: Sections studied showed the cells to be arranged in compact sheets, acinar and nested pattern. The neoplastic cells were round to polygonal with abundant pale staining to clear cytoplasm and centrally located nucleus. Extensive areas of haemorrhage and necrosis was also

noted. The tumour involved the peri- nephric fat margin. No lympho- vascular invasion was noted in the sections taken. The final diagnosis was Clear Cell Renal Cell Carcinoma along with features of Chronic Pyelonephritis.

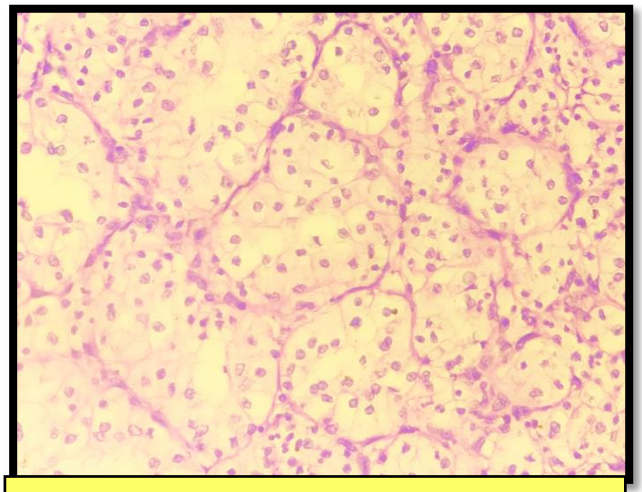

Fig. 7: H & E, 40x Neoplastic cells are round to polygonal with abundant pale staining to clear cytoplasm and centrally located nucleus.

DISCUSSION

Kidneys are one of the major organs of the human body that serve several essential functions. Their main function is to regulate the balance of electrolytes in the blood, along with maintaining pH homeostasis. They also remove waste products of metabolism from blood and produce erythropoietin to maintain hematopoiesis and an important enzyme, renin to maintain blood pressure[1].

Kidneys are affected by various non-neoplastic and neoplastic pathological processes. 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].

Radical or partial nephrectomy is the treatment of choice for a great proportion of patients with renal tumors. Accurate diagnosis of most renal tumours is not possible before surgery, hence a detailed and meticulous histopathological examination of nephrectomy specimen is required to establish the histological type and to evaluate histopathological prognostic determinants i.e. tumor size, histological subtype, nuclear grade and stage in cases of malignant renal neoplasms[2].

Histological subtype according to the Heidelberg classification of Renal cell carcinoma include clear cell ("conventional") adenocarcinoma (80%), papillary (15%), chromophobe (5%), collecting duct (1%), and unclassified (4%). Primary squamous cell carcinoma of the kidney is a very rare entity. The incidence of renal squamous cell carcinoma among renal tumor is in the range of 0.5-0.8%. Wilm's tumor though ranked fifth in frequency among childhood solid tumours yet it is the most common childhood abdominal malignancy[2].

Study by Thakur et al, A Histopathological spectrum of nephrectomy specimens in a tertiary hospital of Raipur, showed that majority of renal cell carcinoma are seen in patients between 31-60 years of age group, while Wilms' tumor was mainly seen in patients below the age of 10 years[2].

A similar study of histopathological spectrum was conducted by Mukhiya et al with 121 cases of nephrectomy specimen. The neoplastic cases were 33 in number (27.27%). Malignant tumours (32 cases) were more as compared to benign cases (one case). Among the malignant ones, clear cell carcinoma (20 cases i.e., 60.6%) was the most frequent.[1]

Udager et al published a review article focusing on a conceptual framework for approaching RCC diagnosis and classification by categorizing RCCs as tumors with clear cytoplasm, papillary architecture, and eosinophilic (oncocytic) cytoplasm[6].

Lobo et al focused on a group of 154 cases of papillary renal cell carcinoma. The data confirmed that the spectrum of RCCs with papillary growth represents a major diagnostic challenge, frequently requiring a second expert opinion[5].

Perrino et al analyses 136 cases of Renal Cell Carcinoma Unclassified with an aim to describe the morphological findings of tumours within this category and to determine the most frequent morphological features leading to classification difficulty. Tumours were assessed for a variety of histological features and assigned to the following morphological groups: predominantly oncocytoma/ chromophobe RCC-like; clear cell RCC-like; papillary RCC-like; collecting duct-like; and pure sarcomatoid differentiation.[7]

Madhu Kumar et al conducted a study with a Total 14 nephrectomy cases were studied in a period of 2 years from 2015 to 2017, in which RCC is most common (10 cases), followed by SCC and Angiomyolipoma, 2 cases each. Most of the patients presented in age group of 4th to 5th decade

with male to female ratio of 1.16:1. Histologically RCC-clear cell type was the most common subtype[3].

Valdair F. Muglia and Adilson Prando published a review article Renal cell carcinoma: histological classification and correlation with imaging findings. Imaging methods play a relevant role in the diagnosis of RCCs, determining a tendency toward the diagnosis of tumors at earlier stages, besides being essential for staging and therapeutic planning.[8]

Srinivasa et al reviewed the 2004 World Health Organization (WHO) classification of RCC, described the cytogenetics of RCC, presented the imaging features of common and uncommon histologic subtypes of RCC, and discussed the effect of accurate histologic classification on prognosis and treatment of RCC. The differences in clinical behavior are likely related to differences in cytogenetic changes and molecular events associated with diverse histologic subtypes of RCC. It is well established that clear cell RCC is associated with a less favorable prognosis compared with papillary and chromophobe carcinoma. Histologic and radiologic profiles of diverse subtypes of RCC can be used as biologic indicators of clinical behavior, response to treatment, and prognosis.[9]

CONCLUSION

Renal Cell Carcinoma is a remarkable tumour, the subtyping of which can put a dilemma on the final diagnosis by a pathologist. The histological classification of Renal Cell Carcinoma plays an important role in the final patient outcome with the prognosis and treatment. While the histopathological examination is the gold standard in the identification of subtype, the radiological contribution should not be discounted in the final diagnosis. With recent advances, a better knowledge and understanding, the challenging differentiation between Clear Cell RCC and ever increasing non- Clear Cell RCCs is identified and acknowledged. An integrated approach to the subject can yield a better medical management.

Abbreviations: H-E: hematoxylin-eosin, RCC: renal cell carcinoma, SCC: Squamous Cell Carcinoma, WHO: World Health Organization.

CONFLICTS OF INTEREST: None.

AUTHOR CONTRIBUTION:

Dr. Reeta Dhar: Conception, Design, Supervision, Materials, Data collection/ processing, Analysis, Literature review, Writer, Critical Review.

Dr. Almas Dalvi: Design, Supervision, Materials, Data collection/processing, Analysis, Literature review, Writer, Critical Review.

Dr. Vrutika Shah: Corresponding author, Design, Supervision, Materials, Data collection/processing, Analysis, Literature review, Writer.

AUTHOR DECLARATION:

• Financial or Other Competing Interests: None

• Was Ethics Committee Approval obtained for this study? NA

• Was informed consent obtained from the subjects involved in the study? Yes

• For any images presented appropriate consent has been obtained from the subjects. Yes

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