



HISTOPATHOLOGICAL SPECTRUM OF RENAL CELL CARCINOMA

Pathology

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ABSTRACT

Background. Renal cell carcinoma have specific histopathological, genetic characteristics & Prognostic markers such as tumor grade, and necrosis or microvascular invasion are useful for determining appropriate follow-up and selecting patients for adjuvant therapy. Hence, the objective of the current study was to evaluate these pathological variables and histopathological spectrum of RCC.

Material and Methods. -107 cases of radical nephrectomy received in Pathology Department, Madras Medical College, were included in this retrospective study. Age, sex, histologic subtype, Fuhrman grade (except for chromophobe RCC, primary squamous cell carcinoma, ewings sarcoma and adult wilms) tumor necrosis and microvascular invasion were determined in all cases.

Results. Clear cell, papillary, chromophobe carcinomas, sarcomatoid, adult Wilms, primary squamous cell carcinoma and ewings sarcoma accounted for 85 (79%), 8(8%), 5(4.6%), 5(4.6%), adult wilms 2(1.8%), 1(0.93%) and 1(0.93%) cases, respectively. Fuhrman grade 2 and pT3 stage were predominant features, tumor necrosis was identified in one third of investigated tumors and microvascular invasion in 9 tumors (8.4%).

Conclusions: Most tumors were clear cell type and had a predilection for G2 and pT3 categories, instead papillary form, the second as frequency, had higher values regarding grading and tumor necrosis, but lower stage. Tumor necrosis correlates with higher grade and tumor stage.

KEYWORDS

Renal, Carcinoma, Variants

Introduction

Renal cell carcinoma (RCC) accounts for over 2.5% of all cancers [1], 2% of cancer mortality [2] and 95,000 deaths per year worldwide [3]. Around 208,500 new cases of kidney cancer are diagnosed in the world each year [4]. The peak incidence is in the sixth and seventh decades of life and the male to female ratio is 1.6:1.0 [5]. Moreover, RCC is a heterogeneous disease comprising different types with specific histopathological and genetic characteristics [10]. The four main subtypes of RCC, as defined by the Heidelberg classification system, are clear-cell, papillary, chromophobe and collecting-duct [10]. In addition, the 2004 World Health Organization (WHO) classification of RCC, also include medullary carcinoma, multilocular cystic RCC, mucinous tubular and spindle cell carcinoma, and unclassified categories [11, 12]. The clear cell type is the most common adult RCC, representing 70% of all RCCs. Papillary RCC accounts for 10%–15%, chromophobe RCC for 4%–6%, renal oncocytoma for 5%, and unclassified lesions for 4%–5% of RCCs. In our study we aimed to evaluate the pathological variables, such as histologic subtype, tumor grade, tumor necrosis, resection margins status and microvascular invasion in with renal cell cancer.

Methods and Materials

This is a retrospective study conducted in the Department of Pathology, at Madras medical college, Chennai. The blocks and slides of all radical nephrectomy excised over a period of five years, from Jan 2011 to Dec 2016, were retrieved and reviewed. All slides were stained with hematoxylin and Eosin stains. The clinicopathologic features including sex, age, tumor size, histologic subtype, growth pattern, nuclear grade, tumor stages, resection margins status, tumor necrosis, and microvascular invasion were evaluated by reviewing the medical records, pathologic slides and reports. Histologic subtypes were classified based upon the 2004 WHO classification [12], and nuclear grading was based on the Fuhrman system [15].

Results

Our study consisted out of 107 consecutive RCCs, examined and diagnosed in the Pathology Department between 2011 and 2016. 70 (65.4%) patients were male, and 37(34.6%) were female (ratio 1.8:1). Regarding patients age distribution, the peak incidence of renal carcinomas was seen in 51-60(30.8%) age group followed by (24.2%) in 41-50 age group. Patients were between 16 and 85 years of age

Table 1: Tumor histology on studied renal cell

Tumor Type	Number of Patients	Percentage(%)
Clear cell RCC	85	79
Papillary RCC	8	8
Chromophobe RCC	4	4.67

Sarcomatoid RCC	4	4.67
Adult wilms tumor	2	1.8
Primary Squamous Cell Carcinoma	1	0.93
Extra Skeletal Ewings Sarcoma	1	0.93

Of the patients studied, the clear cell RCCs (fig: 1) variant was seen in 85(79%) characterized by clear cells with abundant cytoplasm separated by fibrovascular stroma, followed by Papillary RCC 8 (8%) , characterized by papillary arrangement with foamy histiocytes in stalk.

Sarcomatoid renal cell carcinoma accounts for 1% of all adult tumors and it composed of spindle cells. It is usually of aggressive nature generally comes under G4. In our study we reported 5 cases.

According to Fuhrman grading system, 48 tumors corresponding to G2 criteria, 24 tumors with G3, 14 with G1 and 9 in G4. Among the 8 patients with papillary variant, Fuhrman grade 3 was seen in 2 tumors and grade 2 was seen in 4 tumors. Chromophobe RCCs variant was seen in 5 (4.67%) of the patients studied. Fuhrman grading is not appropriate for this tumor.⁶

Renal ewings sarcoma is an extremely rare entity, which has been documented throughout the literature as isolated case reports. It has been reported that most patients presenting with primary Ewings Sarcoma of the kidney which carries a slight preponderance in men, and a worse prognosis if metastases are present at the time of diagnosis [Bing et al. 2009]. We also reported one case in our study in a 42-year male.

Primary squamous cell carcinoma (SCC) of the renal pelvis is an extremely rare entity representing only 0.5% to 15% of all urothelial malignancies. Review of literature shows that only two cases of primary SCC of kidney have been reported to date. 9. We reported a case of squamous cell carcinoma of the kidney in a 65-year male.

Wilms' tumour is very rare in adults with an incidence of about 0.2 per million per year¹³ and represents less than 1%⁷ of all diagnosed renal tumours. We reported 2 cases of adult Wilms in a 16 year and 64 year female respectively.

Owing to inconstant disposable clinical data regarding metastases (M) status, a rigorous classification on pTNM stage could not be achieved for all the patients included in our study.

However, we attempted to characterize the tumors distribution according to pT stage. We noted 50 (46.7%) records corresponding to pT3 stage, 34 (31.7%) to pT1, and 23 (21.49%) to pT2. No records on pT4 stage were noted. Resection margins status, tumor necrosis and microvascular invasion were also evaluated. There were 30 cases in which tumor necrosis was present, tumor necrosis was more present in stage pT3

than pT1 and 2, and also in G3 and 4. 9 tumors had microvascular invasion in our study.

Discussion

RCC is the most common malignancy of the human kidney, with a variable outcome. Currently, tumor stage, size, RCC subtype, and nuclear grade are widely accepted as important pathologic prognostic indicators for RCC [16]. The incidence of RCC in our series was higher in the sixth decade of life, which was similar to previous reports and reviews. The male to female ratio of 1.8:1 seen in our study is close to that of referenced studies⁵.

RCC histologic subtype is the first parameter taken into account for pathologic evaluation. The main histologic subtype encountered in our study was clear cell carcinoma. Histologic subtyping have a clinical relevance for patients outcome. Clear cell RCC have a less favorable prognosis (stage for stage) than do papillary RCC and chromophobe RCC.

Sarcomatoid renal cell carcinoma that is thought to represent the high-grade end of all subtypes, noted in five cases in our study, implies a poor outcome, associated with reduced response to immunotherapy treatments^{11,17,18}. Primary squamous cell carcinoma of kidney, ewings sarcoma and adult wilms tumor are associated with poor prognosis.^{8,9,13}

Although each of the histological variants displays a spectrum of clinical behavior, conventional carcinomas tend to behave aggressively, while chromophobe carcinomas and papillary carcinomas follow a more indolent clinical course¹⁹.

More than half of all investigated cases were G2 tumors in our series. Regarding the Fuhrman nuclear grading system is a well documented and well recognized independent prognostic tool.

One third of investigated tumors showed the presence of necrosis in our study. Necrosis had higher values in papillary form when compared with its presence in clear cell tumors, more specific almost half of papillary tumors, respectively ¼ in clear cell tumors. Also, we demonstrate that RCC tumors with coagulative necrosis tend to exhibit other adverse pathologic features, including high nuclear grade and advanced tumor stage compared with tumors without necrosis. These results are comparable with those of other studies²⁰. Our study also revealed that tumor necrosis correlates with higher grade and tumor stage. The presence of histological necrosis has been shown to be an adverse prognostic feature of clear-cell carcinomas. It has been shown in a recent study to confer a two- to three-fold higher risk of death from RCC than in patients with no tumour necrosis²¹. Histologic coagulative tumor necrosis is an independent predictor for clear cell and chromophobe RCC outcome, and it should be routinely reported and used in clinical assessment²⁰.

Microvascular invasion is a reliable prognostic factor with a high risk for the development of metastatic disease when demonstrated¹⁴. We noted a prevalence of 8.4% in our study, lower than the results of other groups. However, the difference may be explained by the detection method used for microvascular invasion from our study (classical hematoxylin and eosin routine examination) to others (using Factor VIII and/or CD34 staining for this purpose).

Conclusions

By far, the main histologic subtype encountered in our study was clear cell carcinoma. We also found more than half G2 tumors, most cases in pT3 stage and necrosis in one third of evaluated tumors. Different histologic subtypes have different predilections for specific pathologic features, such as pT stage, Fuhrman grade or tumor necrosis. Clear cell tumors were established more often in G2 and pT3 categories, instead papillary form had higher values regarding grading and tumor necrosis, but lower stage. Our study also revealed that tumor necrosis correlates with higher grade and tumor stage.

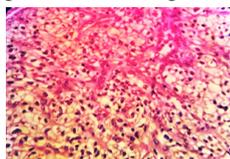


Fig:1 clear cell RCC (40X) shows clear cell with abundant vacuolated cytoplasm and round nuclei

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