Papillary Renal Cell Carcinoma: Clinicopathologic Study of 144 Cases with Emphasis on Subtyping

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ABSTRACT

Background: Papillary renal cell carcinoma (PRCC), a morphologically and genetically distinct subtype of RCC, is morphologically separated into two subtypes for therapeutic and prognostic purposes. In spite of multiple studies, many clinicopathologic issues about PRCC remain vague because the cohorts were small. Our study was designed to review and analyze the clinicopathologic features associated with Type 1 versus Type 2 PRCC.

Design: Our pathology archives were searched for all nephrectomies and kidney tumor biopsies performed between 1985 and 2011, with the final pathologic diagnosis of PRCC. Slides and pathology reports were reviewed. The diagnosis of PRCC was confirmed in each case and subtypes were determined based on established morphologic criteria. Follow-up data was obtained from the clinical database.

Results: We identified a total of 144 cases (74 Type 1, 46 Type 2 and 24 mixed) – 29 female and 115 male. Mean age was 56.0 years for Type 1 and 59.0 years for Type 2 (range, 23-88 years). Mean tumor size: 3.6 cm Type 1 and 4.6 cm Type 2 *(p=0.1)*. Race distribution: 88 white, 45 black, 11 others. Ten patients had metastases (2 Type 1, 6 Type 2 and 2 mixed). None of the tumors showed sarcomatoid differentiation. Desmoplasia was present in 9% of cases while microscopic scar was identified in 45% of cases. Type 1 tumors were more likely to have nuclear grade 2 and less while Type 2 tumors were more likely to have nuclear grade 3 and above *(p<0.001)*. Type 1 tumors mostly presented at stage 1 while Type 2 tumors were more likely to present at higher stages *(p=0.05)*. Perinephric fat invasion *(p=0.004)*, microvascular angiolymphatic invasion and main renal vein invasion were more likely in Type 2 tumors. There was no significant association between tumor type and renal sinus fat invasion or invasion of muscular branches of renal vein. Follow up information was available in 134 patients: 11 alive with disease, 117 alive no disease, 1 dead of disease, 5 dead of other causes. Median follow up time was 58.5 months (range, 1-272 months).

Conclusions: Type 2 tumors are larger. Sarcomatoid differentiation is a rarity in both subtypes. Type 2 tumors have higher nuclear grades and present at higher stages than type 1 tumors. Type 1 PRCC appears to have better clinical outcomes than Type 2. Based on long follow-up data, both subtypes appear to have excellent prognosis when diagnosed at early stage.

BACKGROUND

Papillary renal cell carcinoma (PRCC) is a morphologically and genetically distinct subtype of renal cell carcinoma (RCC) that accounts for 7-20% of cases in different studies. It is typically characterized by a predominant papillary pattern, although various architectural and cytological variations have been described. Two major subtypes have been proposed based on morphologic and immunohistochemical grounds with proposed therapeutic and prognostic implications (**Figures 1** and **2**). Still, available data on the clinical significance of these 2 subtypes is conflicting in many aspects which probably contributed to the discrepancies between different studies in regard to the prognosis of PRCC in comparison to the other histological subtypes of RCC.

DESIGN

The archives of the Department of Pathology at Yale University were searched for all cases of nephrectomy or kidney tumor biopsy between 1985 and 2011. Cases with the final diagnosis of PRCC were selected.

Slides and reports were reviewed and pathological parameters including pathological subtype, tumor size, tumor encapsulation, tumor extent (to include involvement of perinephric fat, renal sinus fat, renal sinus muscular vein or the adrenal gland), nuclear grade, the presence of microvascular angiolymphatic invasion, gross or microscopic necrosis, desmoplasia, microscopic scar, cystic architecture, sarcomatoid differentiation, and lymph node involvement were recorded. Clinical data including patient's age, sex and race, the presence of distal metastasis (clinical stage) and patient's follow up status were also collected from our electronic medical records. Chi-square analysis and ANOVA regression analysis were used for the comparison of qualitative and quantitative variables, respectively. Survival and progression were estimated using the Kaplan-Meier method. Statistical significance was established at p <0.05.

RESULTS

- Total number of cases: 144
- Seventy-four cases of Type 1, 46 cases of Type 2, and 24 cases of mixed Type 1 and Type 2 PRCC
- Twenty-nine female patients and 115 male patients
- Eighty-eight white patients, 45 black, 11 others

Table 1. Clinicopathologic Features of Papillary Renal Cell Carcinoma Subtypes

Clinicopathologic Features	Type 1 (n=74)	Type 2 (n=46)	Mixed (n=24)	p value
Gender Male Female	 64 (87%) 10 (13%)	 34 (74%) 12 (26%)	 17 (71%) 7 (29%)	0.0874
Age (years) (Mean)	56.0	59.0	59.7	N/S
Race White Black Others	 46 (62%) 25 (34%) 3 (4%)	 27 (59%) 12 (26%) 7 (15%)	 15 (63%) 8 (33%) 1 (4%)	0.6025
Size (cm) (Mean)	3.6	4.6	5.8	0.1000
Laterality Left Right NOS	 33 (44%) 39 (53%) 2 (3%)	 25 (54%) 20 (44%) 1 (2%)	 12 (50%) 12 (50%) 0	N/S
Focality Unifocal Multifocal	 60 (81%) 14 (19%)	 44 (96%) 2 (4%)	 20 (83%) 4 (17%)	N/S

Table 2. Pathologic Characteristics of Papillary Renal Cell Carcinoma Subtypes

Pathologic Criteria	Type 1 (n=74)	Type 2 (n=46)	Mixed (n=24)	p value
Fuhrman Nuclear Grade				
1	11 (15%)	0	0	
2	62 (84%)	14 (31%)	4 (17%)	
3	1 (1%)	31 (67%)	15 (63%)	<0.0001
4	0	1 (2%)	0	
Pathologic T Staging				
1	60 (81%)	34 (74%)	12 (50%)	
2	6 (8%)	7 (15%)	5 (21%)	
3	2 (3%)	2 (4%)	3 (13%)	0.5
4	1 (1%)	3 (7%)	0	
Lymph Node Status				
NX	74 (100%)	41 (89%)	20 (83%)	
N0	0	3 (7%)	3 (13%)	N/S
N1	0	2 (4%)	1 (4%)	
Invasion				
Renal Sinus Fat	0	2 (4%)	2 (8%)	N/S
Main Renal Vein	0	2 (4%)	0	N/S
Perinephric Fat	2 (3%)	5 (11%)	3 (13%)	0.004
Angiolymphatic	1 (1%)	2 (4%)	0	N/S
Coagulative Necrosis	21 (28%)	27 (59%)	8 (33%)	0.005
Sarcomatoid Differentiation	0	0	0	N/S
Distant Metastases	1 (1%)	6 (13%)	3 (13%)	N/S
Microscopic scar	28 (38%)	20 (44%)	11 (46%)	N/S
Desmoplasia	2 (3%)	9 (20%)	1 (4%)	N/S

Table 3. Clinical Outcomes in Renal Cell Carcinoma Cases

Clinical Outcome	Alive With Disease	Alive Without Disease	Dead of Disease
Number of Cases	11	117	6

† Average survival: 22 months; Median follow-up time: 58.5 months (range, 1-272 months).

RESULTS

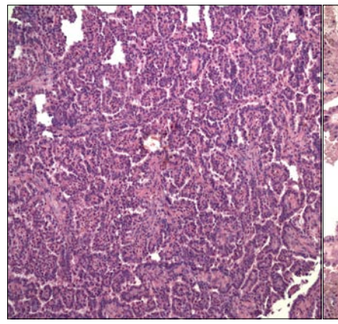

Figure 1. Type 1 PRCC is characterized by papillae covered by a single or double layer of small cells with scant pale cytoplasm and small ovoid nuclei with inconspicuous nucleoli.

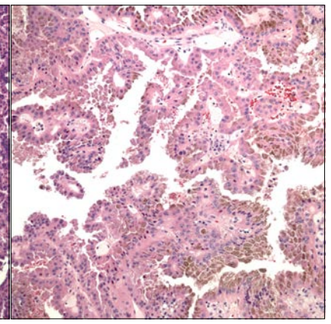

Figure 2. Type 2 PRCC is characterized by large spherical nuclei, prominent nucleoli and nuclear pseudostratification with voluminous eosinophilic cytoplasm.

- Twenty multifocal tumors and 124 unifocal tumors
- Tumor encapsulation was identified in 76 cases.
- None of the cases showed sarcomatoid transformation.
- **Table 1** summarizes the differences between Type 1 and Type 2 PRCC in terms of clinicopathologic features, while **Table 2** summarizes the pathologic characteristics. The clinical outcome data is summarized in **Table 3**.

CONCLUSIONS

- Type 2 tumors are larger.
- Type 2 tumors are more likely to have high nuclear grades.
- Type 2 tumors present at a higher stage of disease.
- Both types have an excellent prognosis with rare cases of death due to the disease.
- Type 1 PRCC appears to have better clinical outcomes.
- Types 1 and 2 PRCC are 2 distinct histological and clinical subtypes of PRCC.
- Although Type 2 presents at a higher stage that Type 1, both subtypes have excellent prognosis when diagnosed at early stage.

REFERENCES

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