Clinicopathologic Characteristics of Renal Cell Carcinoma in Patients 45 Years of Age and Younger

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ABSTRACT

Background: Renal cell carcinoma (RCC) occurs mainly in older people and is infrequently diagnosed in children and young adults. Limited studies have been conducted on RCC in the younger age group, hence the clinical and morphologic spectrum remain incompletely defined, and the behavior is poorly understood. The aim of this study was to analyze the clinicopathologic characteristics of RCC in patients 45 years and younger.

Design: Based on the retrospective review of our files, cases diagnosed as renal cell carcinoma in patients 45 years old and younger in our institution between 1985 and 2011 were identified. Slides in our files were reviewed on all cases. Gross findings were obtained from pathology reports. Follow-up data was obtained from the clinical database.

Results: We identified a total of 102 cases of RCC in patients aged 45 years and younger (63 males, 39 females). Age range: 3-45 years, median age: 40 years. Median tumor size: 3.7 cm (range: 0.5-27 cm). Laterality of tumor was evenly split between right and left. Histologic types: 58 clear cell (CRCC), 24 papillary (PRCC), 11 chromophobe (ChRCC), 5 translocation-associated (TxRCC), 2 multilocular cystic (MCRCC), 1 medullary (MRCC) and 1 mixed. Sixty-six patients underwent radical resections, 33 had partial resections wile three had percutaneous needle biopsies. Tumor was unifocal in 94 cases, and multifocal in 8 cases. Approximately 59% of the tumors demonstrated Fuhrman nuclear grade 2. Pathologic stage at diagnosis: 54 pT1a, 17 pT1b, 14 pT2a, 5 pT2b, 9 pT3a and 1 pT3b. At the time of diagnosis, lymph node involvement, renal sinus fat invasion, main renal vein invasion, perinephric fat invasion and microvascular angiolymphatic invasion were identified in 5, 5, 5, 9, and 11 cases, respectively. Microscopic coagulative necrosis was identified in 33 cases, while sarcomatoid differentiation was present in 7 cases. Distant metastasis was present in 8 cases. Clinical outcome data: 4 alive with disease, 57 alive without disease, 25 alive NOS, 8 dead of disease (10 months average survival, 7 months median survival, 5 male, 3 female).

Conclusion: Although uncommon in children and young adults, RCC is predominantly clear cell type, occurs more commonly in males and mostly has an indolent course. Clear cell and translocation-associated subtypes account for the clinically aggressive cases.

BACKGROUND

Renal cell carcinoma (RCC) is a relatively uncommon entity in younger patients. RCC typically presents in older patients, with the majority of tumors presenting in the fifth to seventh decades of life (median age of diagnosis: 66 years). The incidence of all RCCs is gradually increasing, and diagnosis of the disease is occurring at earlier stages due to the combination of frequent general health screenings and increasing use of ultrasonographic and computed tomographic (CT) modalities. Although overall incidence is increasing, the low frequency of tumors in these younger patients has led to a paucity of definitive literature regarding specific clinicopathologic presentation, disease progression, prognosis and survival. The empirical evidence is limited, but it has been postulated that RCCs in younger patients may represent a distinct clinicopathologic disease state with different disease progression and survival rates. The aim of this study was to evaluate the clinicopathologic parameters of RCC in younger patients in order to assess their effects on clinical progression and subsequent outcomes.

DESIGN

We retrospectively identified data from 102 patients of 45 years of age or less (63 male, 39 female) with documented renal cell carcinoma from our institutional file database between 1985 and 2011. Eligible patients included all histologically proven renal cell carcinoma cases in native kidneys that were treated by radical or patient nephrectomies, or, in rare cases, by percutaneous needle biopsy.

Gross pathologic findings and slide analysis were originally performed by an anatomic pathologist at our institution at the time of diagnosis, and all cases were subsequently reviewed for study. All cases were staged using the 2010 AJCC TNM classification system. Patients were segmented into categories based on histopathologic subtype.

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

Table 1. Clinicopathologic Features of Renal Cell Carcinoma Subtypes

Clinicopathologic Features	CRCC (n=58)	PRCC (n=24)	ChRCC (n=11)	TxRCC (n=5)	Others (n=4)
Gender					
Male	21 (36%)	6 (25%)	7 (64%)	3 (60%)	2 (50%)
Female	37 (64%)	18 (75%)	4 (36%)	2 (40%)	2 (50%)
Age (years)					
(Mean ± SD)	38.1 ± 7.0	37.2 ± 5.8	37.4 ± 5.5	29.6 ± 13.3	34.3 ± 12.5
Size (cm)					
(Mean ± SD)	5.4 ± 4.6	4.5 ± 3.6	6.4 ± 3.4	7.2 ± 1.9	3.7 ± 4.1
Laterality					
Left	29 (50%)	12 (50%)	6 (55%)	3 (60%)	1 (25%)
Right	29 (50%)	12 (50%)	5 (45%)	2 (40%)	3 (75%)
Focality					
Unifocal	53 (91%)	21 (88%)	11 (100%)	5 (100%)	4 (100%)
Multifocal	5 (9%)	3 (12%)	0	0	0

Table 2. Pathologic Characteristics of Renal Cell Carcinoma Subtypes

Pathologic Criteria	CRCC (n=58)	PRCC (n=24)	ChRCC (n=11)	TxRCC (n=5)	Others (n=4)
Fuhrman Nuclear Grade					
1	7 (12%)	2 (8%)	0	1 (20%)	3 (67%)
2	30 (52%)	18 (75%)	10 (91%)	2 (40%)	0
3	15 (26%)	4 (17%)	1 (9%)	2 (40%)	0
4	6 (10%)	0	0	0	1 (33%)
Pathologic T Staging					
1a	33 (57%)	15 (63%)	4 (36%)	0	2 (67%)
1b	8 (14%)	5 (21%)	2 (18%)	2 (40%)	0
2a	8 (14%)	2 (8%)	3 (28%)	1 (20%)	0
2b	3 (5%)	1 (4%)	1 (9%)	0	0
3a	6 (10%)	1 (4%)	1 (9%)	1 (20%)	0
3b	0	0	0	0	1 (33%)
Lymph Node Status					
NX	48 (83%)	23 (96%)	9 (82%)	3 (60%)	2 (50%)
N0	8 (14%)	1 (4%)	2 (18%)	1 (20%)	0
N1	2 (3%)	0	0	1 (20%)	2 (50%)
Invasion					
Renal Sinus Fat	4 (7%)	0	0	0	1 (25%)
Main Renal Vein	4 (7%)	0	0	0	1 (25%)
Perinephric Fat	5 (9%)	1 (4%)	1 (9%)	1 (33%)	1 (25%)
Angiolymphatic	9 (16%)	0	1 (9%)	0	1 (25%)
Coagulative Necrosis	18/35	7/11	6/9	0/1	1/3
Sarcomatoid Differentiation	5/33	1/11	0/7	0/0	1/3
Distant Metastases	2/58	1/24	0/11	3/5	2/4

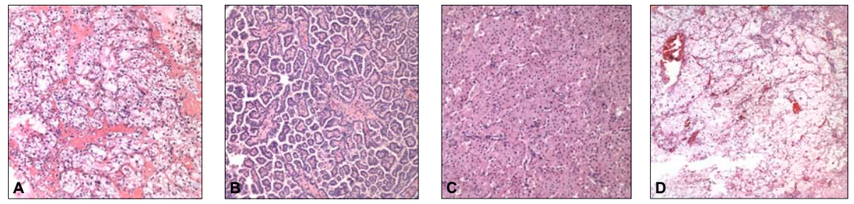

Figure 1: Renal Cell Carcinoma subtypes. **(A)** Clear cell renal cell carcinoma (CRCC); **(B)** Papillary renal cell carcinoma (PRCC); **(C)** Chromophobe renal cell carcinoma (ChRCC); **(D)** Translocation-associated renal cell carcinoma (TxRCC)

Table 3. Clinical Outcomes in Renal Cell Carcinoma Cases

Clinical Outcome	Alive With Disease	Alive Without Disease	Alive NOS	Dead of Disease†
Number of Cases	4	57	25	8

† Average survival: 10 months (± 69.8 months); Median survival: 7 months.

- The most common Fuhrman nuclear grade within all RCC subtypes examined was grade 2 (59%).
- Tumor stage was predominantly pT1 across all RCC subtypes.
- Seventeen out of 102 cases were evaluated for lymph node status for staging purposes. Lymph node metastasis was found in 5 cases.
- Invasion of renal cell carcinoma into adjacent structures was a relatively uncommon occurrence. No particular RCC subtype demonstrated a statistically significant predilection for invasion into extrarenal tissue. Of note, a particularly aggressive case of mixed RCC invaded into all adjacent structures.
- Coagulative necrosis was found in 31% of all cases.
- Sarcomatoid differentiation was found in 15.2% of CRCC; otherwise it was an uncommon feature in other subtypes of RCC).
- Evidence of distant metastasis was found in three out of five TxRCC cases. Distant metastasis was an uncommon finding otherwise. The most common sites of metastatic disease were the liver, lung, and vertebral bodies.
- In terms of clinical outcomes, 94 out of 102 cases had long-term follow-up data present in our institutional database, with eight patients lost to follow-up. Of the 94 cases evaluated, four are currently alive with evidence of active disease and eight died as a result of their disease. Amongst these eight cases, the median survival from time of diagnosis was 7 months and the mean survival time was 10 months.

CONCLUSIONS

The clinicopathologic course of renal cell carcinoma in younger patients may represent a distinct entity in comparison with the course in older patients. Although uncommon in children and young adults, RCC is predominantly clear cell type, occurs more commonly in males and mostly has an indolent course. Clear cell and translocation-associated subtypes account for the clinically aggressive cases in our cohort. The data presented herein displays multiple noteworthy findings, but continued study is necessary in order to better define the potential differences in clinical findings and progression for RCC in young patients.

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