ORIGINAL ARTICLE

Renal Cell Carcinomas: Correlation of Size with Tumor Grade and Extracapsular extension

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ABSTRACT

Introduction: To find the association of tumor size with grade of tumor and its extra capsular extension.

Materials and methods: A review of record of all renal biopsies performed at pathology department King Edward Medical University over a period of two years was done.

Results: It was found that large sized tumors tend to have a higher grade and this correlation was found to be statistically significant (P=0.02). A significant correlation was also seen between the size of tumor and extra capsular extension (P=0.001).

Conclusion: It was concluded patients presenting with larger renal tumors, who subsequently underwent nephrectomy and histopathological analysis were diagnosed with a higher grade. This relation implies that these patients with larger tumors will in turn have poorer prognosis.

Key words: extracapsular extension, tumour grade, renal cell carcinoma

INTRODUCTION

Renal cell carcinoma (RCC) is the most common renal parenchymal malignancy and represents 3% – 6% of all adult malignancies[1]. Patients are generally older than 40 years at diagnosis and the disease occurs predominantly in the seventh decade of life[2]. The clinical behavior of renal cell carcinoma (RCC) is generally unpredictable, and surgery remains the only effective method of treatment for this tumor. Approximately 50% of patients with RCC have poor prognosis[3-7]. Several factors have been examined with respect to their prognostic abilities in RCC including pathologic grade, stage, tumor size, nuclear morphometry, tumor cytogenetics, histomorphology and tumor vascularity[8]. With the advent of the new imaging technologies, more cases of kidney neoplams are diagnosed at earlier stages[9-12]. Since biopsy is not routinely performed for the diagnosis and evaluation of the kidney tumors, size of the tumor and radiographic features can be important in surgeon's decision making. Renal cell carcinoma tumors tend to be spherical and their radiologic and pathologic measurement is easy[13]. There is a lot of data on the relationship of outcome of the tumor with the increase in size of tumor but less can be found on the association of the tumor size with grade of tumor and its extra capsular extension.

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MATERIALS AND METHODS

All patients with renal cell carcinomas treated by radical or partial nephrectomy in 2 years period (1st January 2005 to 31st December 2006) from the case files of the Department of Histopathology King Edward Medical University, Lahore were retrieved for study. The records of the patients were reviewed. The sex, age, side and size of the tumor in each patient were recorded. All the histological slides of the tumor and the uninvolved kidney were reviewed. The nephrectomy specimens were examined using standard methods; the hilar lymph nodes were dissected. The renal veins were opened longitudinally and the kidney was bisected sagittally. Renal capsule or perirenal extension was identified. At least 1 block per centimeter of tumor was taken. The blocks were processed for paraffin sections and stained for hematoxylin-eosin. Additional histochemical stain of Periodic Acid-Schiff was available for chromophobe carcinomas. All pathologic blocks were reviewed by a single expert pathologist. Histological diagnosis was made as RCC according to the classification of the Union Internationale Contre Le Cancer and American Joint Committee on Cancer Workshop[14]. Nuclear grade was assessed using Fuhrman table[15]. In cases with intermediate nuclear grade (i.e., lesions having characteristics of two nuclear grades), lesions were assigned the higher of the two grades. Sizes of the tumors were divided into two groups, group A, 3cm to 7cm and group B, greater than 7cm. The chi-square and student t-test were used for the statistical analysis.

RESULTS

A total of 116 patients underwent total or partial nephrectomies. Amongst them 61 were males (52.6%) and 55 were females (47.4%). The mean age for nephrectomy was 36.80±17.67 years (ranging from 1 to 70 years). There were 33(89.2%) patients with malignant and 4 (10.8%) with benign tumor. The mean age for patients with malignant tumor who underwent nephrectomy was 40.73±21.78 years (range, 2 to 70 years) and for benign was 56.0±9.20 years (range, 45 to 65 years). Size of malignant tumors varied from 3.5 to 20 cm and that of benign from 6.00 to 9.00 cm. Mean size for malignant tumors was 8.76±3.35cm and for benign was 6.86±1.44cm. The benign tumors were not smaller than malignant ones (P value=0.07).

Type	=n	Size, cm (range)
Malignant tumors		
RCC	22 (59.5)	8.45 ± 3.88 (3.5 to 20)
TCC of pelvis	2 (5.4)	7.75 ± 1.06 (7 to 8.5)
Wilms tumor	7 (18.9)	10.14 ± 1.95 (8 to 14)
Metastatic SCC	1 (2.7)	9.00
Sarcoma	1 (2.7)	6.50
Benign tumors		
Adenoma	1 (2.7)	6.00
Oncocytoma	2 (5.4)	7.75 ± 1.77 (6.5 to 9)
Leiomyoma	1 (2.7)	6.00
Total	37 (100)	8.55 ± 3.24 (3.5 to 20)

Sizes given in mean ± standard deviation (range)
RCC (renal cell carcinoma), TCC (transitional cell carcinoma), SCC (squamous cell carcinoma)

Out of 33 patients diagnosed with malignant tumors, 22 were of renal cell carcinoma (RCC). 13 were males (59.1%) and 9 were females (40.9%). Mean age for patients with RCC who underwent nephrectomy was 50.14±12.12 years (range 25 to 70 years). RCC was observed more on the right side (63.7%).

The data showed that the grade of the tumor increased with the increase in the size of the tumor, P=0.02 which is statistically significant.

Grade	Tumor size		Total
	Group A (3cm to 7cm)	Group B (>7 cm)	
1	2	0	2
2	5	3	7
3	3	7	10
4	1	1	2
Total	12	10	22

RCC with an extracapsular extension had a mean size of 13.83±4.26cm and the ones with no invasion; mean size was 7.12±2.45cm. A significant co-relation was seen between the size of the tumor and extracapsular invasion. (P=0.001)

DISCUSSION

Renal cell carcinoma is one of the unpredictable neoplasms with a poor prognosis. Identification of patients with a particularly high tumor progression risk level is of great interest from an oncological and surgical point of view. In this context, tumor related prognostic factors include several gross and microscopic findings[17]. Our data showed a lesser incidence of benign tumors as compared to malignant. Frank et al reported that the size of the tumor forms criteria to differentiate benign from malignant tumors[12]. In our study, we found that the increase in the size of the tumor does not precisely refer to its malignancy.

Many investigators demonstrated that just tumor stage and grade had the most important prognostic factors in RCC cases[4,5,17,18]. Further studies implicated the tumor grade as an important prognostic factor[3,19]. Inomiya et al[19] also compared grades 1 and 3 and showed by multivariate analysis that tumor grade is an independent prognostic factor. Smaller tumors generally portend higher postoperative survival rates[20], with various statistically significant break-points reported[9,20]. Our aim was not to duplicate these efforts, but to correlate size of renal cell carcinoma with factors that may independently effect management and outcome of the tumor. We correlated tumor size with Fuhrman nuclear grade and extracapsular spread (T3 or T4 status), all of which have been validated as independent prognostic factors[9]. A higher grade of the tumor was seen in group B (lesions greater than 7cm) and smaller tumors were statistically different from larger ones in nuclear grade.

Nuclear grading according to the Fuhrman classification system [15] is widely accepted and has been shown to confer prognostic significance. A sharp increase in metastases and a decrease in survival have been noted for patients with lesions that are nuclear grade 3 or 4[21]. TNM tumor staging is even more predictive than the Fuhrman classification system. Capsular transgression defines a T3 lesion, with a significant increase in metastases and a decrease in survival for patients with T3 or T4 lesions[22]. Rate of extracapsular extension was found to be significantly higher in tumors larger than 7cm than in smaller ones. This holds significance in making decisions for partial or radical nephrectomy surgeries.

CONCLUSION

In kidney tumors, size was not form a differentiating point between malignant and benign growths. In RCC, tumor size was related to the nuclear grade and extracapsular extension

REFERENCES

1. Landis SH, Murray T, Bolden S, et al. Cancer statistics, 1998. *CA Cancer J Clin.* 1998;48:6–29.
2. Cao Y, Paner GP, Perry KT, Flanigan RC, Campbell SC, Picken MM. Renal neoplasms in younger adults: analysis of 112 tumors from a single institution according to the new 2004 World Health Organization classification and 2002 American Joint Committee on Cancer Staging System. *Arch Pathol Lab Med.* 2005;129:487–491
3. Elfving P, Mandahl N, Lundgren R, Limon J, Bak-Jensen E, Ferno M, et al. Prognostic implications of cytogenetic findings in kidney cancer. *Br J Urol* 1997; 80: 698-706.
4. Bonsib SM. Risk and prognosis in renal neoplasms: A pathologist's prospective. *Urol Clin North Am* 1999; 26:643-660.
5. Nurmi MJ. Prognostic factors in renal carcinoma: An evaluation of operative findings. *Br J Urol* 1984; 56:270-275.
6. Masuda H, Kurita Y, Fukuta K, Mugiya S, Suzuki K, Fujita K. Significant prognostic factors for 5-year survival after curative resection of renal cell carcinoma. *Int J Urol* 1998; 5: 418-422.
7. Guinan PD, Vogelzang NJ, Fremgen AM, Chmicl JS, Sylvester JL, Sener SF, et al. Renal cell carcinoma: Tumor size, stage and survival. Members of the Cancer Incidence and End Results Committee. *J Urol* 1995; 153: 901-903.
8. Dinney CP, Awad SA, Gajewski JB, Belitsky P, Lannon SG, Mack FG, et al. Analysis of imaging modalities, staging systems, and prognostic indicators for renal cell carcinoma. *Urology* 1992; 39: 122-129.
9. Lau WK, Cheville JC, Blute ML, Weaver AL, Zincke H. Prognostic features of pathologic stage T1 renal cell carcinoma after radical nephrectomy. Urology.2002;59:532-7.
10. Luciani LG, Cestari R, Tallarigo C. Incidental renal cell carcinoma-age and stage characterization and clinical implications: study of 1092 patients (1982-1997).Urology. 2000;56:58-62
11. Patard JJ, Rodriguez A, Rioux-Leclercq N, Guille F, Lobel B. Prognostic significance of the mode of detection in renal tumours. BJU Int. 2002;90:358-63.
12. Frank I, Blute ML, Cheville JC, Lohse CM, Weaver AL, Zincke H. Solid renal tumors: an analysis of pathological features related to tumor size. J Urol. 2003;170:2217-20.
13. Guinan PD, Vogelzang NJ, Fremgen AM, et al. Renal cell carcinoma: tumor size, stage and survival. Members of the Cancer Incidence and End Results Committee. J Urol. 1995;153:901-3.
14. Storkel S, Eble JN, Adlakha K, et al. Classification of renal cell carcinoma: Workgroup No. 1. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). Cancer. 1997;80:987-9.
15. Fuhrman SA, Lasky LC, Limas C. Prognostic significance of morphologic parameters in renal cell carcinoma. Am J Surg Pathol. 1982;6:655-63.
16. Ozer E, Yorukoglu K, Sagol O, Mungan U, Demirel D, Tuzel E, et al. Prognostic significance of nuclear morphometry in renal cell carcinoma. *BJU Int* 2002; 90:20-25.
17. Vasavada SP, Novick AC, Williams BR. p53, bcl-2 and Bax expression in renal cell carcinoma. *Urology* 1998; 51:1057-1061.
18. Bretheau D, Lechevallier E, de Fromont M, Sault MC, Rampal M, Coulange C. Prognostic value of nuclear grade of renal cell carcinoma. *Cancer* 1995; 76: 2543-2549.
19. Inomiya H, Isaka S, Okano T, Shimazaki J, Igarashi T, Matsuzaki O. Prognostic factors in patients with non-metastatic renal cell carcinoma. *Nippon Hinyokika Gakkai Zasshi* 1996;87:1099–104
20. Gettman MT, Blute ML. Update on pathologic staging of renal cell carcinoma. *Urology*2002; 60:209 –217
21. Ficarra V, Righetti R, Marignoni G, et al. Prognostic value of renal cell carcinoma nuclear grading: multivariate analysis of 333 cases. *Urol Int* 2001;67:130 –134
22. Tsui K, Shavarts O, Smith RB, et al. Prognostic indicators for renal cell carcinoma: a multivariate analysis of 643 patients using the revised 1997 TNM staging criteria. *J Urol*2000; 163:1090 – 1095.