Microvessel density in Renal Cell Carcinoma

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Summary:

Background: Prognostic histological evaluation of many cancers have recently concentrated on angiogenesis.

Materials &Methods: A total of twenty formaline-fixed, paraffin embedded blocks of renal cell carcinoma were included in this study. Sections were subjected for immunohistochemical staining of CD34. The median of the MVD of all cases of RCC were obtained to divide the cases into high- and low-MVD score groups and were correlated with the tumor stage and grade**.**

Results: there was a significant correlation of the high MVD score with tumor stage (P=0.02).

Conclusion: MVD may be considered as a potential prognostic marker for RCC.

Keywords: CD34, MVD (Microvessel density), RCC (Renal Cell Carcinoma).

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Introduction:

Renal cell carcinoma (RCC) has a relatively low incidence of 3% among other human tumors, nevertheless; it is the most frequent renal neoplasm (90-95%) in adults. The etiology and pathogenesis of RCC has not been completely elucidated. It is more common in men than women with a male-to-female ratio of about 1.6:1. (1) Angiogenesis refers to the generation of new blood vessels from preexisting microvasculature. This process is not only essential to tumor growth but has a relevance to other biological properties of the tumor including its metastatic potential. (2). Microvascular density (MVD) is an often quantified variable of tumor angiodenesis. Recent reports suggest that increased MVD is associated with poor outcome in several malignancies, including breast, prostate, lung, and nasopharyngeal cancers (3–5). Our aim in this study was to assess the importance of MVD in renal cell carcinoma through estimating its median level & determining what this has to do with some of the prognostically recognized clinicopathological variables.

Materials and Methods:

From March 2009 through January 2010, a total of twenty patients with RCC were enrolled in this study. Their relevant formaline-fixed, paraffin embedded tumor tissue blocks were retrieved from histopathological laboratories of Baghdad teaching hospitals and The Hospital of Specialized surgeries. Two sections were prepared from each block; one for hematoxyline-esosine staining; these were examined to review the original diagnosis. The other was utilized for immunohistochemical staining of CD34 according to the manufacturer instructions (Dako Cytomation LSAB+System-HRP immunostaining kit) that utilizes a refined avidin biotin technique.Regarding CD34 scoring, the most vascularized areas (hotspots) within each section were selected at X100 for quantification of blood vessels at a magnification of ×400. A total of five fields were analyzed. Any brown-staining of endothelial cells cluster that was considered as a single, countable microvessel. MVD in the non tumor areas of the section was evaluated as well, and was taken as an internal control. The mean value of the vessel counts in the selected spots was considered as the final MVD value. The median of the MVD of all cases of RCC were stratified to divide the cases into high- and low-MVD score groups (6).

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Results:

A total of twenty cases of RCC were included in this study. Nine (45 %) were males and 11 (55%) were females. Their ages ranged between 30 and 76 years. The values of MVD varied between 19.0 and 36.4 with a median of 27.7 in RCC tumor areas which was significantly higher than the control (P<0.5) . As shown in table (1), there was a significant correlation of the high MVD score with tumor stage (P=0.02).

Table (1): MVD score in relation to different criteria in RCC.

criteria	MVD score		P value
	Low	High	
Age			1.000
More50	5	6	
Less 50	5	4	
total	10	10	
Sex			0.406
Male	3	6	
Female	7	4	
Total	10	10	
Grade			.087
II	10	6	
III	0	4	
Total	10	10	
Stage			.002
T1	7	0	
T2	3	7	
T3	0	3	
Total	10	10	

Pearson Chi-Square
However, no statistically significant association was observed between MVD score and other variables such as the grade of the tumor, age or sex of the patients (p= 0.087, P= 0.406 & P= 1.00 respectively).

A B

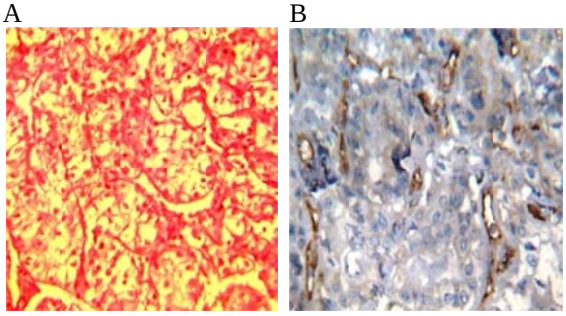

Figure (1): A- H & E staining of RCC. B- Immunostaining of endothelial cells with CD34 marker in RCC (X400).

Discussion:
Angiogenesis, the growth of new blood vessels, has a critical role in tumor growth and metastasis. The purpose of this study was to investigate the involvement of angiogenesis in the pathogenesis of renal cell carcinoma (RCC) through quantitative evaluation of CD34 immunohistochemical expression. The value of MVD as a predictor of prognosis in RCC is controversial. Several reports have shown a positive correlation between MVD and survival or prognosis (7–9). These observations support our findings that high MVD score is significantly correlated with the tumor stage; as all cases of RCC stage T1 revealed low MVD score while all cases of stage T3 showed high MVD score. However, some researchers have reported an inverse relationship (10, 11), and still others were unable to find a significant correlation between MVD and survival (12, 13). These contradictory results from different researches probably require the immunohistochemical application of a combination of other vascular markers like CD31, VEGF, CD105 as well as the application of molecular techniques. In conclusion, our findings indicated that MVD can be considered as a potential prognostic marker for RCC.

References:
1-Kashyap MK, Kumar A, Emelianenko N ,Kashyap A, Kaushik R, Huang R, et al. Biochemical and molecular markers in renal cell carcinoma: an update and future prospects. Biomarkers 2005 Jul;10(4):258-94.

2-. Folkman J, Kalluri R. Tumor angiogenesis. In: Kufe DW, Pollock RE,WeichselbaumRR, Bast RCJ, GanslerTS, Holland JF, Frei EI, editors. Cancer medicine. Hamilton (Ontario, Canada): B.C. Decker, Inc.; 2003. p. 161-94.

3-. de laTaille A, Katz AE, Bagiella E, et al. Microvessel density as a predictor of PSA recurrence after radical prostatectomy. A comparison of CD34 and CD31. Am JClin Pathol 2000;113:555-62.

4-. KatoT, Kameoka S, KimuraT, NishikawaT, Kobayashi M.The combination of angiogenesis and blood vessel invasion as a prognostic indicator in primary breast cancer. BrJ Cancer 2003;88:1900-8.

5-. MineoTC, Ambrogi V, Baldi A, et al. Prognostic impact of VEGF, CD31, CD34, and CD105 expression and tumour vessel invasion after radical surgery for IB-IIA non-small cell lung cancer. J Clin Pathol 2004; 57:591-7.

6 Yao X, Qian C, Zhang Z, et al. Two Distinct Types ofBlood Vessels in ClearCell Renal Cell Carcinoma Have Contrasting Prognostic Implications Clin Cancer Res 2007;13(1):161-169.

7. Zhang YH, Yang Q, Cui W, Liu YX, Liu SX, Yao X.Correlation of microvascular density and clinicopathological factors in different subtypes of renal cell carcinoma. Zhonghua Zhong Liu Za Zhi. 2010 ;32(2):117-22.

8. MineoTC, Ambrogi V, Baldi A, et al. Prognostic impact of VEGF, CD31, CD34, and CD105 expression and tumour vessel invasion after radical surgery for IB-IIA non-small cell lung cancer. J Clin Pathol 2004; 57:591-7.

9. Edwards BK, Brown ML,Wingo PA, et al. Annual report to the nation on the status of cancer,1975-2002, featuring population-based trends in cancer treatment. JNatl Cancer Inst 2005;97:1407-27.

10. Joo HJ, Oh DK, KimYS, Lee KB, Kim SJ. Increased expression of caveolin-1and microvessel density correlateswithmetastasis and poor prognosis in clear cell renal cell carcinoma. BJUInt 2004;93:291- 6.

11. Nativ O, Sabo E, Reiss A, et al. Clinical significance of tumor angiogenesis in patients with localized renal cell carcinoma. Urology1998;51:693- 6.

12. MacLennan GT, Bostwick DG. Microvessel density in renal cell carcinoma: lack of prognostic significance. Urology 1995;46:27-30.

13. Minardi D, Lucarini G, Mazzucchelli R, et al. Prognostic role of Fuhrman grade and vascular endothelial growth factor in pT1a clear cell carcinoma in partial nephrectomy specimens. JUrol 2005; 174:1208 -12.