ORIGINAL ARTICLE

To Study the Expression of Cyclin D1 in Renal Cell Carcinoma

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ABSTRACT

Aim: To observe the expression of cyclin D1 as prognostic marker in different variants of RCC.
Setting: Postgraduate Medical Institute, Lahore
Methodology: Non-probability, Purposive sampling.
Inclusion criteria: Histopathologically diagnosed cases of Renal cell carcinoma of all ages and both gender.
Exclusion criteria: Patients already taking chemotherapy, radiotherapy or hormone therapy.
Results: Patients of >50 years of age are mostly involved (53.8%), with M: F ratio is 1: 1. Clear cell RCC is the most common type i.e., 72(77.4%). As far as CyclinD1 expression score is concerned, 60 (64.4%) cases having score 1 and 2 i.e. up to 30% +ve cells and 33(35.5%) cases having score 3 and 4.
Conclusion: This study showed that the cyclinD1 protein is over expressed in RCC and that high protein levels were related to a better clinical result as well as to most of the good prognostic markers for RCC.
Key words: cyclinD1, RCC

INTRODUCTION

Renal malignancies are a group of cancers derived from tubular epithelium and showing prominent properties thus resulting from various genetic problems[1]. In adulthood, kidney cancer comprises of malignant tumors arising from the parenchyma of kidney as well as pelvis of the kidney. Main kidney cancer i.e. mostly adenocarcinoma type of renal cell malignancy originate from parenchyma of the kidney. Pelvis of the kidney shows transitional cell malignancy mainly[2].

In a study by Donnellan and Chetty, it is shown that cyclin D1 levels within the tumor i.e. intra tumoral cyclinD1 were associated with the disease prognosis for many cancers. In breast carcinoma, the over expression of cyclinD1 was correlated with positive steroid receptors of sex, favorable histological features and good prognosis[5]

METHODOLOGY

This descriptive study was conducted at Postgraduate Medical Institute, Lahore after approval from the Ethical Committee. 93 cases are calculated and confidence level is 95% with margin of errors 10%. Expected %age of subjects with positivity is 41% among the RCC. Non-probability, Purposive sampling technique was used.

RESULTS

The detail of results is given in tables 1, 2, and 3

Table 1: Age distribution

Age (years)	n	%age
< 50	38	40.8
51-69	50*	53.8
>70	05	05.4
Total subjects	93	100%

Statistical Analysis: *P< 0.01 (Highly significant)

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Table 2: Gender distribution

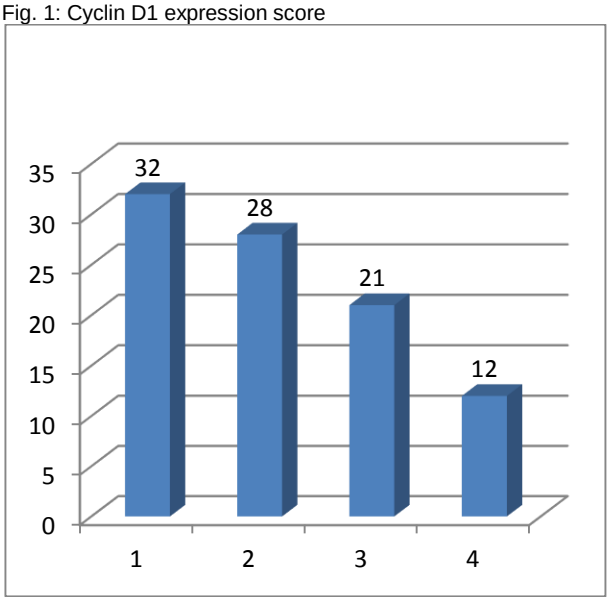
Gender	n	%age
Males	49	52.7
Females	44	47.3
Total subjects	93	100%

Table 3: CyclinD1 Expression Score

Cyclin D1 Score	n	%age
1 (Zero% +ve cells)	32*	34.4
2 (30% +ve cells)	28*	30.1
3 (30-60% +ve cells)	21	22.6
4 (>60% +ve cells)	12	12.9
Total subjects	93	100%

Statistical Analysis: *P< 0.01 (Highly significant)

Fig. 1: Cyclin D1 expression score



DISCUSSION

CyclinD1 was over expressed in RCC samples and negative in controls. This over expression had association with clinical features having prognostic values for RCC in an inverse manner. Cyclin D1 histochemical analysis revealed haphazard staining in positive nuclei and periphery of tumor was marked mostly. This irregular staining of nuclei was also seen in a study by Aaltoma et al[3]. These authors also documented that in areas of worse histology, there is increased intensity and numbering of stained cells. Thus, these results show the values of performing more extensive sampling of RCC. It is for good assessment of histological markers and also for selecting the most aggressive parts of tumors.

Low score cyclinD1 patients of RCC possessed a bad clinical outcome, large size of tumor, positive symptoms at the time of diagnosis, greater Fuhrman nuclear grade, necrosis on histopathology and sarcomatoid features in the tumor and also decreased survival rate having no metastasis resulting in mortality by renal cancers. When performing analysis for clear cell RCC only, this also showed same statistical difference as that of the total subjects of RCC[4].

In a study by Donnellan and Chetty, it is shown that cyclin D1 levels within the tumor i.e., intra tumoral cyclinD1 were associated with the disease prognosis for many cancers. In breast carcinoma, the over expression of cyclinD1 was correlated with positive steroid receptors of sex, favorable histological features and good prognosis[5]

Hedberg et al (1999)[6] observed in 80 patients having RCC and it is seen that in a large number of tumors, there are increased cyclinD1levels. Association of shorter survival is with low protein contents of cyclinD1. CyclinD1 was an important protein for clear cell RCC after multivariate analysis. By the addition of cyclinD1, staging and nuclear grades were used as clinical and pathological indicator in different analysis[7]. This study also showed that use of cyclinD1 is early detector of metastasis especially in clear cell RCC. It is also associated with low protein expression. In early tumor growth, there is an increase in cyclinD1. It is also seen that cyclinD1 is involved in the early events of malignant conversion and cyclinD1 expression decreased as there is progression of tumor. This showed the association between over expression of cyclinD1 and absence of spread or with small sized tumor. This association was observed by Hedberg et al (2004)[6].

Certain events lead to the deposition of cyclinD1 in tumor cell nuclei i.e. translocation of chromosomes, amplification of genes, normal intracellular traffic interruption and decreased proteolysis[8]. Hedberg et al (2004)[6] studied 133 patients of RCC and observed cyclinD1 gene amplification frequency by FISH technique and there are no signs of gene amplification.

A protein is produced which is called cyclinD1b by the polymorphism of G/A 870. This protein causes deposition of cyclinD1 by reducing process of proteolysis. This type formed the active complex with CDK4[9]. In cancer development, CyclinD1 is important cell cycle regulator. The correlation between tumor growth aggression and cyclinD1 over expression has been seen in different cancers, e.g., lung cancer of non small cell type, malignancy of esophagus and head and neck tumors[5] Recently, a few researches have observed the histo pathological role of cyclinD1 in RCC with different results[6].

It is shown that expression of cyclinD1 is seen in RCC and higher values of protein were correlated with better outcome. It is due to that there are many genetic disorders which are seen in renal cell cancers related to genes of specific types. CyclinD1 over-expression may represent important cell-cycle abnormalities in renal-cell carcinomas.

CONCLUSION

Our study shows that the Cyclin D1 protein is over expressed in RCC and that high protein levels are related to better outcome of patient as well as to the most favorable prognostic marker for RCC. Cyclin D1 protein expression, can increase the predictive accuracy of the current prognostic models for RCC.

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