Summery

This study aims first at evaluation of prognostic value of MUC- 1 expression and AgNORs expression. Second, to compare and correlate the findings with other cinicopathological variants such as age, sex, tumor grade and stage. Statistical analysis and correlation were made for all these variants.

This retrospective study was carried upon 50 selected Egyptian patients with different types of RCC . Sex cases of normal kidney tissue were taken as control .The patients were admitted to National Cancer Institute ,Cairo University and Benha University Hospital during the years 1993-2005.

The selected RCC cases included 20 clear cell RCCs, 11 papillary RCCs, 7chromophobe, 6 Bellini duct carcinoma (BDC) and 6 sracomatoid types. The studied cases included 28 male cases and 22 female cases with age ranged from 24 upto 79 years. The mean age was 53.8

Studied cases were graded according to Fuhrman grading system . RCC were divided into : six cases of grade 1, 16 cases of grade 2, 13 cases of grade 3 and 15 cases of grade 4 .Most of studied clear cell RCC (11 cases) and papillary RCC (6 cases) were low grade (G1&G2). Four cases of chromophobe RCC were grade 2 , while four cases of both BDC and sarcomatoid RCC had high grade (G3 & G4 respectively) .

TNM staging system was applied for each tumor case. Lymph node metastases and distant metastases were evaluated for every cases.

As regarding TNM staging, there were 5 cases of stage I , 10 cases of stage II , 21 cases of stage III and 14 cases of stage IV . Six cases of chromophobe RCC and 4 cases of BDC were stage III . Four case of sarcomatoid RCC were stage IV. Among 50 studied cases , 28 cases had no lymph node spread and 22 cases showed lymph node metastases. Concerning distant metastases, 31 cases had no distant metastases , and19 cases showed distant metastases.

MUC-1 was detected by immunohistochemistry staining technique. It appears as circumferential membranous staining or/and diffuse cytoplasmic staining in tumor cells. In all control cases , the epithelial lining of the distal convoluted tubules , collecting tubules and loop of henle showed membranous staining with apical polarity .

Among 50 studied cases of RCC only 4 cases were negatively stained for MUC-1 . Four cases were (1): 10-25% of tumor cell positive ,8 cases were (2): 26-50% of tumor cells positive , 18 cases were (3) : 51-75% of tumor cells positive and 16 cases were (4) :>75% of tumor cell positive . Six cases of chromophobe were (2) . All cases of BDC and 5 case of sarcomatoid RCC recorded high score (3 & 4) . The nuclear grading and the tumor stage were considered as independently prognostic factors.

A statistically significant correlation between MUC-1 expression on one hand and nuclear grade on the other hand was detected . All of grade 1 cases were recorded low score (1 & 2) , in the same time revealed pure staining pattern (membranous in clear RCC and papillary RCC or cytoplasmic in chromophobe) .All cases of grade 4 showed mixed

pattern (circumferential membranous staining with additional cytoplasmic pattern), and 11 cases had (4) score .

There was a statistically significant correlation between MUC-1 expression and the tumor stage .As All cases of stage I had a low score (1&2) and pure expression pattern. On the other hand the mixed staining pattern and high sore (3&4) were detected in all cases of stage IV

The proliferative activity was evaluated by AgNORs stain .the mean AgNORs count for control and malignant cases was detected by counting the numbers of dots in nuclei of 100 cells in high power fields (x100). For control cases , the mean AgNORs was 2.1 dots/nucleus. It was 5.6 dots/nucleus in clear cell RCC and 5.3 dots /nucleus in papillary type .The lowest one was detected in chromophobe type (4.7 dots/nucleus) ,and the highest ones were observed in BDC and sarcomatoid type (7.3 and 8.4 dots/nucleus, respectively) .

A significant correlation was found between the mean AgNORs count and both tumor grade and stage . The studied cases with low grade and stage showed lower AgNORs count than cases with higher grade and advanced stage. The mean AgNORs count of both grade 1 and stage I were 2.6 , 1.4 dots/nucleus respectively. While it was 9.1 dots/nucleus in stage IV and 9.3 dots/nucleus in grade 4.

One-year survival was recorded for all cases ,18 cases were disease free within one year after nephrectomy , 13 cases were recurrent and 19 cases had died. Four cases of chromophobe were disease free ,while 5 cases of sarcomatoid had died and four cases of BDC were recurrent .

This study could find a statistically significant correlation between the one –year survival one side and both of the tumor grade and stage on the other side. Half of grade 1 (3 cases) and 9 cases of grade 2 were disease-free . the morbidity/mortality rate was increased with higher grades , 13 cases of grade 4 had died and 7 cases of grade 3 were recurrent. Concerning the stage, 2 cases of stage I and 6 cases of stage II were disease –free , 9 cases of stage III were recurrent and 10 cases of stage IV had died.

One-year survival was significantly correlated with the MUC-1 expression . Two cases of score (1) and 8 cases of score (2) were disease free while 10 cases of score (4) had died. Regarding, the pattern of expression , half of pure cytoplasmic staining cases (2 cases) and 10 cases of pure membranous staining were disease -free . the mixed paterrn showed poor prognosis ,as 15 cases of circumferential pattern with additional cytoplasmic staining had died and 7 cases were recurrent .

The AgNORs count was significantly associated with one –year survival .The disease- free cases has the lowest mean count (3.6 dots/nucleus) . the died cases showed higher count (7.9 dots/nucleus)

Our study could find a significant correlation between MUC-1 expression and AgNORs count . The mean AgNORs count was gradually increased with MUC-1 score . It was 3.5 dots/nucleus in score 1 and 8.4 dots/nucleus in score (4). Concerning the pattern , Pure membranous patter had the lowest ANORs count (3.7dots/nucleus) while the circumferential pattern with additional cytoplasmic staining had 7.7 dots/ nucleus

`Conclusion

- MUC-1 may be used to differentiate between the non-neoplastic and neoplastic kidney lesions. Its extent and expression may detect the aggressive behavior of tumors.

- MUC-1 expression is higher in BDC and sarcomatoid types.

- The advanced stage and higher grade cases show higher expression and mixed staining patterns.

- The disease –free cases have a lower MUC -1 score and pure staining patterns ,comparing the recurrent and/or died cases .

- Silver colloidal staining for AgNORs may be differentiate between non-neoplastic and neoplastic kidney lesions .It also

could used to detect the grade and the stage of RCC and help to determine the hisopathological types .

- Mean AgNORs count /nucleus is higher in sarcomatoid type and BDC .the higher grade and advanced stage have a higher AgNORs count. The poorer the prognosis of RCC shows increased AgNORs count than the disease free cases .

Recommendation

- Simultaneous determination of MUC-1 and AgNORs is more serviceable than either alone for the precise predication of metastases status and survival of RCC.

- It is recommended that to repeat this study with longer period of survival .This step not be carried out because of lack of data.

- As regarding the other types of RCC, this study was limited by few numbers of cases from types of RCC rather than clear cell carcinoma. It was recommended to repeat this study with larger numbers of these types..