Chapter 7

Summary & Conclusions

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In Egypt, carcinoma of the prostate is, by far, the most common malignant tumour of the male genital organs. It ranks the 5th most common tumour of all male cancers and the second after bladder cancer in patients over the age of 60 years.

Adenocarcinoma of the prostate gland presents with a wide variety of clinical findings, ranging from asymptomatic, relatively latent tumours to highly aggressive, metastasizing cancers.

Once the disease has spread beyond the surrounding fibrous capsular region of the gland, treatment is often unsuccessful. The main issues for clinicians and pathologists involved in prostate cancer are early detection of the prostate and identification of the prognostic factors that predict outcome in individual patients.

In this study, 100 cases with prostate cancer that were obtained by needle biopsy (34 cases), Transurethral Resection Prostatic (TURP) chips (29 cases) and prostatectomy specimens (37 cases)], were submitted to: Histopathologic examination for typing, grading (WHO nuclear grading and Gleason Sum Score), and pathologic staging.
Immunohistochemical analysis for detection and evaluation of CD44, MIB-1, and p21 proteins.

All 100 cases were acinar carcinomas of the peripheral zone, of which 76 cases were of low-nuclear grade and 24 of high-nuclear grade, 52 of low-G.S.S. and 48 of high-G.S.S. TNM staging could be accessible in only 37 cases, of which 18 cases were of pT-2, 12 of pT-3, and 7 of pT-4.

This study revealed high significant correlations between histopathologic pattern and that of G.S.S. and nuclear grade($p<0.01$) and between G.S.S. and nuclear grade($p<0.01$).

Also this work showed a highly significant correlation between both G.S.S. and nuclear grade and that of pathologic stage($p<0.01$) in examined prostatectomy cases with prostate cancer.

The present study, evaluated the expression of CD44(as an adhesion molecule), MIB-1(as a proliferative marker), and p21 (as a cell-cycle regulator) proteins in the examined cases with prostate cancer, in an attempt to determine their prognostic significance.

Regarding CD44 expression, there was a decreased CD44 expression with evolution into high-grade tumours [either nuclear grading ($p<0.05$) or G.S.S ($p<0.01$)].

This study also reported that reduction of CD44 expression was proportionate to pathologic stage and lymph node status in prostatectomy cases ($P<0.01$), suggesting that evaluation of expression levels of this gene may eventually become useful in predicting prognosis and determining appropriate therapy for prostate cancer.

The findings of this study suggest the low proliferative activity of prostate cancer (only 27 cases showed MIB-1 expression >15%).
Although the direct correlation between the proliferative activity of prostate cancers examined as measured by MIB-1 expression and both nuclear grade and G.S.S. does not reach statistical significance, there was a direct significant correlation between proliferative activity and pathologic stage ($p<0.05$)

Regarding p21 immunoreactivity, the findings of the current work were encouraging, as p21 immunoreactivity was inversely correlated with both G.S.S. and nuclear grade ($p<0.01$), although, the inverse correlation between p21 expression and pathologic stage does not reach statistical significance. However, reduced expression of p21 protein could be a reliable prognostic marker for detecting progression.

Considering correlation of associated expression , the present work revealed a highly significant direct correlation between $p21^{WAFI/CIPI}$ negativity and decreased CD44 expression *($p<0.01$)*. While MIB-1 expression was inversely correlated with either CD44 expression or $p21^{WAFI/CIPI}$ imunoreactivity, however ,these correlations did not reach statistical significance.

The present study also revealed that there was a high significant inverse correlation between histopathologic pattern and p21 expression ($P<0.01$), however its correlation with either MIB-1 and CD44 expressions didn't reach statistical significance .

Conclusions:

I. Reduction of CD44 expression in prostate cancer was closely related to the aggressive biological behaviour.

Based on a radical prostatectomy, a CD44 score of <10% could be identified with a sensitivity of 86%. If CD44 tumour scores can be determined reliably using biopsy specimen, a combination of this score with clinical parameters may enhance the ability to predict N.component prior to surgery.

II. The marked difference in CD44 expression that was observed in comparing non-metastatic with metastatic carcinomas to lymph nodes suggests that CD44 should be investigated as a molecule that may play a role in the pathogenesis of prostate cancer metastasis.

III. Regarding MIB-1 expression, we vote with those insisting on the low proliferative nature of prostate cancer, and it seems premature to recommend routine clinical application of this marker, , being aware of the importance of the balance between cell proliferation and cell loss rate which characterizes tumour cell kinetics.

IV. Frequent expression of p21 protein in well-differentiated lesions may support a favourable prognosis of the tumours with p21 over-expression as increased p21 expression leads to cell growth arrest and is accompanied by the development of morphologic and phenotypic markers of senescence in some or all cells.

V. It is unknown whether p21 antibody used in this study detects a mutant, wild-type, or both forms of the gene. Further study in conjunction with molecular analysis is necessary to determine the biological role of p21 in prostatic carcinogenesis.

IV. Both CD44 and p21 could be used as valuable prognostic parameters in prostate cancer and their associated expression may provide additional prognostic advantage for undetermined cases of aggressive potentiality.