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Immunohistochemical Detection of Breast Cancer Antigen I and P63 in Prostate Tumors among Sudanese Patients

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***Abstract**: This is analytical retrospective case control hospital based study aimed to detect BRCA1 and P63 expression in prostate tumors among Sudanese patients usingimmunohistochemistry. Forty paraffin embedded blocks previously diagnosed as prostate tumors were selected forth is study. Samples included 20( ) benign tumors samples and 20(50) malignant tumors, the malignant samples grade were moderately and poorly differentiated tumors, with frequencies of 9(45%) and 11(55%) respectively. Sections of µ were cut from each paraffin block then stained by immunohistochemical method for detection of BRCA1 and P63. The data obtained was analyzed using SPSS program version 20, mean, frequency, and chi square test were calculated. The patient's age ranged between 36 and 100 years with a mean age of 73 years. Most patients were more than 50 representing 38(95%) patients and the remaining 2(5%) patients were less than or equal 50 years. BRCA1 showed negative expression in all samples. P63 positive expression was found in (4/20) in malignant samples, and (16/20) samples showed negative expression, while in benign samples (20/20) showed positive expression, this result showed significant association between p63 expression and prostate tumors (P.value =0.000) The study concluded that expression BRCA1 is negative in all samples. P63 expression is associated with benign type of prostate tumors.*

Keywords— BRCA 1; P63; Prostate tumors.

1. INTRODUCTION

Prostate cancer, also known as carcinoma of the prostate, is the development of cancer in the prostate. Prostate is a gland in the male reproductive system. Most prostate cancers are slow growing; however, some grow relatively quickly [(1)].

Prostate cancer is the sixth most common cancer in the world and accounts for 9.7% of cancer in men. It is the leading causes of new in men and is second only to lung cancer as a cause of cancer related deaths in men [(2)].

Prostate cancer is the most common cancer in Sudanese men. The age standardized rate is 10.3 and mortality is 8.7 per 100,000 population .It ranked second among all cancers in both sexes after breast cancer [(3)].

BRCA1 is a multifunctional tumor suppressor protein implicated in regulating the maintenance of genome integrity through the activation of DNA repair genes, heterochromatin formation, double-strand-break repair, homologous recombination events, and ubiquitination [(4)].

Mutations in BRCA1 have been associated with increased risk of breast, ovarian, and more recently, prostate cancer – particularly high grade disease [(5)]. BRCA1 protein expression in prostate differentially regulates IGF-IR gene expression in an androgen-dependent manner and found significantly elevated BRCA1 levels in prostate cancer in comparison with normal prostate tissue [(6)].

The p63 gene encodes six protein isoforms. The transactivating isoforms has similar actions with p53, while the N-isoforms inhibit transcription activation by p53 and Trans activating isoforms. P63 is expressed in stratified epithelia and basal cells of the prostate and salivary glands. In mammary epithelium p63 has been show to express only in the myoepithelial layer [(7)].

2. Materials and methods:

2.1 Materials:

Archived tissue blocks of prostate tumors were used in this study.

2.2 Methods:

2. 2.1 Study design:

This is hospital analytical retrospective case control study aimed to detect protein expression BRCA1 and p63 in prostate tumors by using immunohistochemistry.

2.2.2 Study samples and processing:

Forty tissue blocks obtained from prostate tumors samples, twenty samples previously diagnosed as prostate cancer and twenty samples which previously diagnosed as benign tumors were selected for this study. Patient's identification data (age, histopathological diagnosis, and grade) were obtained from the patients files. Sections of µ thickness were cut by rotary microtome, mounted in positively charged glass slides and put in a oven

2.2.2.1 Immunohistochemical staining:

Immunohistochemical staining was carried out using monoclonal mouse anti human BRCA 1, clone MS110, isotype; IgG1 and p63 clone 4A4, isotype; 1gG2a/Kappa. Tissue sections (µ) were deparaffinized in xylene and rehydrated in graded alcohol (100%, 90%, 70%, and 50%) and water two minutes for each. Antigen retrieval was performed by using PT link water bath with citrate buffer (pH6.8), and then slides section were circulated by Dako pen, were incubated for 10 minutes in 3% hydrogen peroxide to block endogenous peroxidase activity. The

slides were treated with anti p63 primary antibody for p63 expression and by anti BRCA1 primary antibody for 20 minutes and washed in phosphate buffer saline (pH7.4). Then treated with secondary biotinylated antibody for 30 minutes, and washed in phosphate buffer saline (pH7.4). After that the avidin peroxidase complex was added for 15 minutes. Then slides were incubated in 3, 3 diamminobenzidine tetra hydrochloride (DAB) H2O2 mixture for 7 minutes to visualize the reaction and washed in water. Finely slides were counterstained in Mayer's hematoxylin stain for 1minute, dehydred, cleared and mounted in DPX mounting media [8].

2.2.3 Data analysis :

Data was analyzed by using 20 SPSS computer program. Frequencies, means and chisquare test values were calculated.

2.2.4 Ethical consideration:

Sample collected after taking ethical acceptance from hospital administration .

RESULTS

The study included forty samples, 20(50%) of them were benign prostate hyperplasia while 20(50%) were prostatic adenocarcinoma a (Table 1).

The patient age ranged between 36 and 100 years with a mean age of 73 years, and standard deviation 12.04, patients age equal or less than 50 years representing 2(5%) and the remaining 38(95%) were more than 50 years (Table 2).

The malignant samples grades were moderately and poorly differentiated tumors, with frequencies of 9(45%) and 11(55%), respectively (Table 3).

No expression in all benign and malignant samples stained with BRCA1 nuclear gene.

P63 positive nuclear expression was found in 4/20 malignant samples, while 16/20 samples showed negative result. All benign samples 20/20 showed positive nuclear expression, this result showed significant association (P. value =0.000) (Table 4).

Table (1): Distribution of histopathology diagnosis among study samples:

Histopathology diagnosis	Frequency	Percent (%)
Malignant	20	50
Benign	20	50
Total	40	100

Table (2): Distribution of age group among the study population:

Age group (Years)	Frequency	Percent (%)
Equal or less 50	2	5
More than 50 38	38	95
Total	40	100

Table (3): Frequency of cancer grade:

Cancer grade	Frequency	Percentage (%)
Moderate differentiated tumor	9	45
Poor differentiated tumor	11	55
Total	20	100

Table (4): Relation between p63 expression and histopathological diagnosis of prostate tumors:

Expression of p63	Histopathological diagnosis		Total	P. value
	Benign	Malignant		
Positive	20	4	24	0.000
Negative	0	16	16	

DISCUSSION

Prostate cancer is one of most significant problems occurring worldwide. The present study involves 40 cases of prostate lesions applied for immunohistochemical stains for BRCA1 and p63. Concerning the age group of study population, the patient's age ranged between 36 and 100years with a mean age of 73years, which explain that the risk of prostate cancer increases with the age. This study result ts consistent with Bostwick *et al*.[9],who reported that risk of developing prostate cancer increases quickly over the age of 50 in white men and over the age 40 in black men. Agree also with Galani, [1], who reported that prostate cancer is predominantly a disease of older men (aged 65 – 79 years).Also agree with Elamin et al. [3], who reported that mean age of prostate patients was 72.2 +- 9.25.

All benign samples showed negative expression in BRCA1, that agree with the observation by Schayek et al. [6], found that, BRCA1 was not expressed in normal prostate tissue. Localization of BRCA1 only to the most aggressive tumors may reflect an inefficient attempt to up regulate DNA repair mechanisms in prostate epithelial cells. All malignant samples showed negative expression, agreed with BRCA1 negative prognostic factor in PCa, independent to tumor grade, stage, formalin fixation interval and long term fixation which may result in Ag deficiency and need large sample size and new samples Castro, *et al*.[10].Disagreed with studies reported BRCA1 mutation carriers to have a significant increased relative risk of developing prostate cancer Ford *et al*. [11].

The expression of p63 revealed that there was significant association between marker expression in benign prostate tumors and this may be due to shedding of secretory cells leaving basal cells.

This study agreed with Signoretti *et al*. [12], who reported that p63, is a reliable prostate basal cell marker and that the Np63 isotype is the most abundantly represented in normal prostate basal (PrEC) cells. Because P63 protein is consistently undetectable in prostate cancers. Also agreed with Baig *et al*. [2], in which their study concluded that prostatic adenocarcinoma were p63 negative and the most of the benign ambiguous lesions of prostate were p63 positive.

Agreed with Signoretti *et al*. [12], reported that all basal cells express p63; therefore, this marker can be useful in distinguishing benign lesions from prostate malignancy.

References

1. Galani, P. Diagnosis and prognosis of prostate cancer. *Journal of Advanced Medical and Dental Sciences Research*. 2015. 3(5):49-53.
2. Baig, MK., Hassan, U. and Mansoor, S. Role of p63 in Differentiating Morphologically Ambiguous Lesions of Prostate. *Journal of the college of Physicians and Surgeons Pakistan*. 2012. 22 (12):773-777.
3. Elamin, A., Ibrahim ME., Abuidris, D., Mohamed, KEH. and Mohammed, SI. Part I: cancer in Sudan burden, distribution, and trends breast, gynelogical, and prostate cancers. *Cancer medicine*. 2015. 4(3):447-456.
4. Chen, J., Silver, DP. and Walpita, D.Stable interaction between the products of the BRCA1 and BRCA2 tumor suppressor genes in mitotic and meiotic cells. *Mol Cell*. 1998. 2(3):317–328.
5. Agalliu, I., Gern, R., Leanza, S. and Burk, RD. Associations of high-grade prostate cancer with BRCA1 and BRCA2 founder mutations. *Clin Cancer Res*, 2009. 15(3):1112–1120.
6. Schayek, H., Haugk, K., Sun, S., True, LD., Plymate, SR. and Werner, H. Tumor suppressor BRCA1 is expressed in prostate cancer and controls insulin-like growth factor I receptor (IGFIR) gene transcription in an androgen receptordependent manner. *Clin Cancer Res*. 2009. 15(5):1558–1565.
7. Stefanou, D., Batistatou, A., Nonni, E., Arkoumani, N., Agnantis., J. p63 expression in benign and malignant breast lesions. *Histol Histopathol* . 2004. 19(2):465-71.
8. Bancroft, JD. and Marilyn, G. Theory and practice of histological techniques,2008 6th ed. Churchill Livingstone, London, pp 125.
9. Bostwick, DG., Burke, HB., Djakiew, D., Euling, S., Ho, SM., Landolph, J. and Morrison, H. Human prostate cancer risk factors, *Cancer journal*, 2004. 101(10):2371-2390.
10. Castro, E., Goh, C. and Olmos, D. Germline BRCA mutations are associated with higher risk of nodal involvement, distant metastasis, and poor survival outcomes in prostate cancer. *J Clin Oncol*. 2013.31 (14):1748-1757.
11.Ford, D., Easton, DF., Bishop, DT., Narod, SA. And Goldgar ,DE. Risks of cancer in BRCA1-mutation carriers, Breast Cancer Linkage Consortium. *Lancet*, 1994.343:692–695.
12. Signoretti, S., Waltregny, D., Dilks, J., Isaac, B.,Lin, D., Garraway, L., Yang,A., Montironi, R., Mckean, F. and Loda, M. P63 is a prostate basal cell marker and is required for prostate development. *The American journal of pathology*. 2000.157(6):1769-1775.