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Correlation Expression of Livin Apoptosis Inhibitor Marker in Sudanese Patient with Prostate Cancer

ABDALWHAB A. ALI
MSc student at Faculty of Medical Laboratory Sciences, Alneelain University, Khartoum, Sudan
AGEEB M. HASSAN
MD – Pathology/Assistant Professor, Sudan International University (SIU) Khartoum, Sudan

Abstract:

To explore the expressions of Livin in prostatic cancer and the correlation among them. Totally 27 paraffin-embedded prostate cancer tissues obtained from patients who were performed with rectal prostate biopsy or excision and 23 paraffin-embedded prostatic hyperplasia tissues were collected as control group. All the specimens were confirmed by pathology. Immunohistochemistry method was used to detect the expressions of Livin in prostatic cancer and compared to hyperplasia tissues. The positive expressions of Livin in prostatic cancer tissue were higher than prostatic hyperplasia tissues (88.9%, 47.8%, $P < 0.05$). The study concluded that the Immunohistochemical staining with the Livin could improve the diagnostic performance and helped in avoid carrying out new biopsies in prostate cancer detection. Therefore we propose that this marker can be applied along with other prostate cancer as diagnostic factors.

Key words: Prostate cancer, livin, correlation

1. INTRODUCTION:

Benign prostatic hyperplasia (BPH) is the most common disorder affecting men worldwide and the most common cause

of lower urinary tract symptoms. BPH and clinically associated lower urinary tract symptoms/dysfunction, is a common disease of elderly men affecting 50 to 90% of all men between 50 and 80 years of age[1]. Prostate cancer PCa is one of the most important cancers in men. With a worldwide incidence of 25.3 per 100,000 it is the second most common cancer in men, with large differences between countries. Important clues on risk factors remain to be found. Age, genetic factors and environmental influences have been studied. Incidence has been increasing over the last few decades, largely due to early detection procedures. The mortality rate of 8.1 per 100,000 mainly affects men at older age[2]. This is found in a study of general autopsy of the male elderly over 50 years old that the morbidity has been increasing with the patients get older. The correlation between age and prostate is accepted by all researches[3],[4]. Patients with prostatic cancer have no obvious symptoms in early stage, but when cancer tissue increases to a certain extent which leads to suppression of the urethra, and the abnormal urination. For example, dysuria and hematuresis occur in a small number of patients, while the distant metastasis such as mostly bone metastasis is found in a large number of patients. It is in advanced stage that patients feel lower back pain, which with poor therapeutic effect and unfavorable prognosis.

Apoptosis regulatory proteins are playing important role in the occurrence and development of tumors. At present, it is believed that gene directly control the occurrence and development of tumor cell apoptosis and other gene expressions. Through signal transduction, gene products activation is influenced by extracellular factors and indirectly regulates cell apoptosis finally[5],[6]. The inhibitor apoptosis protein IAP family is characterized by one or more repeats of a highly conserved 70 amino acid domain termed the baculoviral IAP repeat (BIR) and suppress apoptosis triggered by a wide variety of stimuli, including viral infection, chemotherapeutic

drugs, staurosporin, growth factor withdrawal, and by components of the tumor necrosis factor-α (TNF-α)/Fas apoptotic signaling pathways[7, 8]. Expression of Livin inhibited apoptosis by a number of stimuli; whereas an antisense construct was shown to induce apoptosis. Like its other family members, Livin was capable of binding to caspases and could inhibit the proteolytic processing of caspase-9 in vitro. Restricted expression of livin mRNA during development and transformed cell lines suggests a very specific role for Livin. Therefore, inhibitors of Livin could be useful adjuncts to chemotherapy in the treatment of malignancies as prognostic factor[9].Our previous study showed that, as a member of the IAP family, Livin might play an important role in the initiation of human prostate cancer and promote cell proliferation by regulating the G1–S cell cycle transition[10]. Another previous report by our group showed that Livin directly regulates prostate cancer cell invasion by impacting the nuclear factor-kappaB (NF-kB) signaling pathway and the expression of FN and CXCR4, resulting in the inhibition of FAK, Src, and a5 and b3 integrins[11]. The interpretation of these data suggested that Livin may be a potential therapeutic target to regulate the development and progression of prostate cancer.

Therefore, in this study, Immunohistochemical staining method was used to detect the expressions of Livin marker for the diagnosis of prostatic cancer and the scientific experimental basis were applied for the effective targets in the treatment of prostatic cancer.

2. MATERIAL AND METHODS:

2.1. Slides preparation:

A total of 50 sections of 4µm thickness were obtained from paraffin embedded tissue (previously diagnosed by H&E) from RADIO AND ISOTOPE CENTER OF KHARTOUM (RICK),

using a rotary microtome and taken in thermal coated slide and dried in hot plate oven at 80ºC for one hour.

Patients were divided into two groups: 27 paraffin-embedded prostate cancer PCa specimens obtaining from patients performed with rectal prostate biopsy or excision. And 23 paraffin-embedded prostatic hyperplasia BPH specimens obtaining from patients performed with excision were selected as control. All specimens were confirmed by pathologist and have complete clinical and pathological data.

2.2. Immunohistochemical staining:

Sections were incubated overnight after being deparaffinized in xylene and rehydrated in ethanol at 50°C. To perform heat-induced antigen retrieval the sections were placed in 10 mM citrate buffer (pH 6.0) and heated to a boil. Endogenous peroxidase function was quenched using peroxidase blocking solution. Section treated with primary rabbit anti-human Livin polyclonal antibodies (1:100) for thirty minutes, then sections were incubated with streptavidin horse radish peroxide (SA-HRP)-conjugated goat anti rabbit secondary antibodies for 30 min, then treated with 3,3'diaminobenzidine (DAB) for seven minutes , then washed in phosphate buffer saline for five minutes, then counter stained in Mayer's haematoxylin for one minute and washed in water and blued in 0.05% ammoniated water for 16 seconds, then washed in tap water , dehydrated through ascending grades of ethanol (50%,70% ,90%, 100%) two minutes for each then cleared in two change of xylene two minutes for each, and mounted in DPX mounting media[12].

2.3. Result Interpretation:

Results obtained were detected by researcher and confirmed by experienced pathologist.

Negative and positive controls were used for evaluation of the test sections.

Ethical clearance for this study is provided by ethical committee of AL-Neelain University -faculty of medical laboratory science and Radio And Isotope Center Of Khartoum (RICK).

2.4. Data analysis:

The data were analyzed using version 18 SPSS computer program, frequencies, means and chi-square values were calculated.

3. RESULT:

In this study population distributions of patients are benign prostate hyperplasia BPH and prostate cancer PCa. The results showed that, 21 (42 %) of the 50 patients were positive, while that 29 (58 %) of the 50 patients were negative (**Table 1**).

3.1. Computation biology software (SPSS)

Questionnaires of 50 participants were analyzed and the results show in the following tables.

The frequency of benign prostate hyperplasia BPH patients according to age groups, showed that 4.3% (1/50), 13% (3/50), 43.5% (10/50) and 39.1% (9/50) individuals, for the age groups (less than 54 yrs), (55-64 yrs), (65-74 yrs) and (above the 75 yrs) respectively. By the same token, through frequency of prostate cancer PCa patients according to age group 11.1% (3/50), 18.5% (5/50), 18.5% (5/50) and 51.9% (14/50) individuals, for the age groups (less than 54 yrs), (55-64 yrs), (65-74 yrs) and (above the 75 yrs) respectively (**table 2**). By the same token, distribution of the results among diagnosis and age group were summarized in (**Tables 3 and 4**).

Table 1: immunohistochemical results:

Result	Frequency	Percent
Positive	35	70.0
Negative	15	30.0
Total	50	100.0

Table 2: relation between age group and diagnosis:

Age group		Diagnosis		
		BPH	PCa	Total
less than 54	Count	1	3	4
	% within age group	25.0%	75.0%	100.0%
	% within diagnosis	4.3%	11.1%	8.0%
55-64	Count	3	5	8
	% within age group	37.5%	62.5%	100.0%
	% within diagnosis	13.0%	18.5%	16.0%
65-74	Count	10	5	15
	% within age group	66.7%	33.3%	100.0%
	% within diagnosis	43.5%	18.5%	30.0%
over 75	Count	9	14	23
	% within age group	39.1%	60.9%	100.0%
	% within diagnosis	39.1%	51.9%	46.0%
Total	Count	23	27	50
	% within age group	46.0%	54.0%	100.0%
	% within diagnosis	100.0%	100.0%	100.0%

Table 3: Relation between diagnosis and results:

Diagnosis		Results		
		Positive	Negative	Total
BPH	Count	11	12	23
	% within diagnosis	47.8%	52.2%	100.0%
	% within results	31.4%	80.0%	46.0%
PCa	Count	24	3	27
	% within diagnosis	88.9%	11.1%	100.0%
	% within results	68.6%	20.0%	54.0%
Total	Count	35	15	50
	% within diagnosis	70.0%	30.0%	100.0%
	% within results	100.0%	100.0%	100.0%

Table 4: relation between age group and results:

Age group		Results		
		Positive	Negative	Total
less than 54	Count	3	1	4
	% within age group	75.0%	25.0%	100.0%
	% within results	8.6%	6.7%	8.0%
55-64	Count	6	2	8

	% within age group	75.0%	25.0%	100.0%
	% within results	17.1%	13.3%	16.0%
65-74	Count	9	6	15
	% within age group	60.0%	40.0%	100.0%
	% within results	25.7%	40.0%	30.0%
over 75	Count	17	6	23
	% within age group	73.9%	26.1%	100.0%
	% within results	48.6%	40.0%	46.0%
Total	Count	35	15	50
	% within age group	70.0%	30.0%	100.0%
	% within results	100.0%	100.0%	100.0%

4. Discussion:

Prostate cancer PCa is one of the most important cancers in men. With a worldwide incidence of 25.3 per 100,000 it is the second most common cancer in men[2].

In this study patient's age ranged from 47 to 96 years mean age 61.5, the result showed there was an increase susceptibility of prostate cancer PCa with increasing age. This finding was supported with (Zhang, Qian et al. 2013)[3], who reported that Larger prostate volumes were positively associated with increased age.

In this study 88.9% (24/27) of prostate cancer PCa patients expressed of livin with significant P value (0.002), 47.8% of benign prostate hyperplasia BPH patients expressed Livin, this finding compatible with (Gu, J., L. Ren, et al. 2015) [13], who reported that the positive expression rates of Livin in prostatic cancer 93.02% (40/43), and 64.70% (11/17) positive expression with prostatic hyperplasia . And agreed with (Song, T., B. Hong, et al. 2008) [14], who reported that the Livin gene was highly expressed in neoplastic prostate. And supported with (Chen, F., D. Yang, et al. 2012) who reported there is significant association between the Livin and prostate cancer PCa [11].

CONCLUSION:

The study concluded that the Immunohistochemical staining with the Livin could improve the diagnostic performance and helped in avoid carrying out new biopsies in prostate cancer detection. Therefore we propose that this marker can be applied along with other prostate cancer as diagnostic factors.

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