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Research Article

Surveillance for Early Detection of Prostate and Testicular Cancers in Immunocompetent Younger Men

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ABSTRACT

Aim: To early detection of prostate cancer (PC) and testicular cancer (TC) in young men by cancer biomarkers before development to advanced stages.

Method: Sera from 810 immunocompetent young individuals was analyzed for detecting the levels of alpha-fetoprotein (AFP), human Chorionic Gonadotropin (hCG), and lactate dehydrogenase (LDH) as indicators of testicular cancer and prostate-specific antigen (PSA) for prostate cancer.

Result: Elevated levels of AFP, hCG, and LDH were found in 3, 2, and 8 individuals respectively, but with an insignificant value from the total number. The level of PSA was slightly elevated in two individuals.

Conclusion: Prostate cancer and testicular cancer have not been detected in volunteer men. None of involved men had elevated levels of all of three biomarkers of testicular cancer. The PSA level was not high enough to predict the presence of prostate cancer (PC).

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Introduction

Testicular cancer (TC) is one of the germ cell tumors (GCTs) with 95% originating from the testis [1, 2]. It is considered a relatively rare type of men's cancer, which represents 1-1.5% of all cancers in men [3, 4]. At ages 15 to 35 years, TC is very common and is mainly classified into seminoma and non-seminomatous germ cell tumors (NSGCT) [1, 2, 4, 5]. Three tumor markers, comprising alpha-fetoprotein (AFP), human Chorionic Gonadotropin (hCG), and lactate dehydrogenase (LDH), are very important indicators for the diagnosis of TC before starting treatment or before and after orchiectomy [1, 4]. Although many types of cancer induce elevated levels of those markers, each marker is thought to be specific for one cancer type. For TC, the accuracy of diagnosis will be increased when three markers are measured in the same individual. AFP, which is mainly produced in high concentrations during fetus development, is mainly used for diagnosis of hepatocellular carcinoma in adults [6-8]. The second marker, hCG, belonging to the glycoprotein family of cystine knot growth factors, is normally active in women during early pregnancy through supporting of progesterone secretion [9-11]. It is usually found in very low concentrations (<5 U/I) in men and when the concentration is high, it indicates the presence of TC [4, 12,

13]. Lactate dehydrogenase (LDH), which is the third TC marker, is considered a nonspecific biomarker for cancer diseases. High levels are observed in the serum of approximately 60% of NSGCT with advanced diseases and in 80% of patients with advanced seminoma [14]. Prostate cancer (PC) is another type of cancer that affects various ages of men. In 2007, about 218,890 cases of PC were recorded in the USA with the death of 27,050 persons [4]. For detection of PC, prostate-specific antigen (PSA) representing a kallikrein protease is the most commonly used [15-18]. In order to detect testicular and prostate cancers in younger men, the levels of AFP, hCG, and LDH were investigated for early diagnosis of TC, while measurement of PSA was used as indicator for diagnosis of PC.

Methods

I Sample Collection

Serum samples were collected from the blood of 810 immunocompetent volunteer young men at mean age of 21 years in April 2018. Hemolytic and lipemic sera were eliminated from the collection samples.

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II Reagents

Liquid UV detection kit of lactate dehydrogenase (LDH) and ELISA kits of alpha-fetoprotein (AFP), human Chorionic Gonadotropin (hCG), and prostate-specific antigen (PSA) were purchased from Human Gesellschaft für Biochemica und Diagnostica mbH (Germany).

III Assay

The ELISA technique was used to analyze the serum samples containing AFP, hCG, and PSA antigens. The assay depends on the high affinity of the system biotin-Streptavidin. Absorbance of the final product was measured at 450 nm within 30 min by a BioTek ELx800 ELISA reader (U.S.A). The concentrations of tested samples were obtained by means of a calibration curve, which was established from the calibrators supplied with the kit. LDH levels were measured by using a liquid UV method that was modified based on the recommendations of the Scandinavian Committee on Enzymes (SCE). Briefly, 20 µl of each patient serum was mixed first with 1000 µl of buffer (pH 7.35) supplied by the manufacture and incubated for 1-5 min at 25° C. A volume of 250 µl of substrate composed of NADH (0.75 mmol/l) and sodium azide (0.095%) was added to the mixture. After mixing, the absorbance at 340 nm was read by UV-Visible spectrophotometer (CECIL, CE 1021, England) after 1 minute. Expected normal value of AFP, hCG, PSA antigen, and LDH in healthy individuals is <8.5 ng/ml, <5 IU/l, <4 ng/ml, and 160-320 U/l, respectively.

IV Statistical Analysis

Data of all tests were expressed as mean ± SD. The number of patients with high value was analyzed statistically with total number by “t” test. The value $p < 0.01$ was considered as statistically significant.

Table 1: Number of younger men with high levels of tumor markers for testicular and prostate cancers.

Tumor marker	Patients No. (%)	Concentration	Total No.
AFP	3 (0.96)	100 ng/ml	3
hCG	2 (0.64%)	10-25 IU/I	2
LDH	8 (2.58)	160-320 U/I	8
PSA	2 (0.64)	5 ng/ml	2
Total No.	15		15

Mean ± SD, * Significant differences at $P < 0.01$

Results

For diagnosis of TC, the levels of three biomarkers were measured in the blood of 810 healthy young men. High levels of AFP, hCG, and LDH had been shown in 3(0.96%), 2(0.64%), and 8(2.58%) individuals, respectively. An elevated value of AFP was found within the range of 100-120 ng/ml in three individuals, while a high level of hCG was within 10-25 IU/l in two individuals. The eight individuals who had high values of LDH had a value within the range of 500-525 U/l (Table 1). However, high values of these three markers were not found together in a single individual. The PSA level as indicator for PC was found slightly high in two younger men with none exceeding 5 ng/ml.

Discussion

Although the percentage prevalence of TC is usually very low compared with other men's tumors, it is very common in men aged 20 to 35 years. Thus, routine examination for TC in this specific age of human life is considered a priority for early detection and treatment of such type of cancer. Measurement of both AFP and hCG is usually suggested for early detection of TC because their production is stimulated by the growth of TC [5]. LDH is another marker that also can be used as an indicator for TC. Its level is mostly elevated in the presence of various malignant or benign conditions. Its application together with AFP and hCG will give more accuracy for detection of TC [4, 5]. However, the concentration of three markers in serum is mainly dependent on histological type and cancer stage [4]. Both AFP and hCG, especially beta hCG (hCGβ), are considered valuable markers for diagnosis of two types of TC either before treatment or 5-7 days after orchiectomy [2-4]. However, the diagnosis of non-seminomatous TC, as mentioned by the American Society of Clinical Oncology, usually depends on the measurement of three markers, while LDH and hCG are useful in seminoma TC [1, 4]. The hCG, which is a glycoprotein belonging to the family of cystine knot growth factors is encoded by six non-allelic hCGβ genes [9, 19].

It is normally secreted at high levels in pregnant women to perform many endogenous functions, while its level is absent or very low in men [9, 10, 20, 21]. It plays an important role in spermatogenesis via LH receptor [21]. Moreover, it can be used as a treatment for oligospermia and many other testis function disorders [21]. Thus, the increasing level of hCG especially in young men usually indicates the presence of TC [4]. Moreover, detection of beta subunit of hCG (hCGβ) is more significant than alpha subunit for diagnosis of all types of TC [13]. This is because hCG alpha subunit is most similar to other hormones, unlike beta subunit [9]. However, highest level of hCG was found in 15-20% of advanced seminomatous GCT and in 40% of advanced non-seminomatous GCT [1]. Although some testis disorders or cancers, other than TC, cause elevation of hCG levels, serum hCG level is still essential in the diagnosis of TC, especially when TC is responsible for most of testicular malfunctions [1, 4, 12, 20]. LDH, which is produced by various types of tissues in the human body, is considered a nonspecific marker [5].

Its concentrations can elevate in the presence of many benign and malignant conditions such as many metastatic cancers, hematologic malignancies or infection [22]. LDHC which is one of three LDH subunits (A, B, and C) in sperm cells that are encoded by three genes *Ldha*, *Ldhb*, and *Ldhc*, is important for aerobic glycolysis to generate energy for sperm motility and capacitation [23]. The level of total LDH or LDH-1 isoenzyme has been found elevated either in the presence of TC or without clinical features of TC [2, 3, 24]. However, the high level of LDH is observed in 40-60% of each type of TC (seminoma and non-seminomatous) [1, 4]. From our results, the number of individuals with high levels of LDH was insignificant compared with the total number of young men sampled. Although the fewest number of individuals from our survey had higher values of selected markers for diagnosis of TC, none had elevated levels of more than one marker. Thus, we cannot confirm the presence of TC at any of those individuals and the elevation of one selected marker may result from another disorder.

The presence of the PC in our group of young men can be excluded due to the high level of PSA found in two individuals was not high enough to predict the development of PC. Moreover, the PSA test alone is not always significant for diagnosis of PC [16]. Individuals with a normal value of PSA does not exclude the presence of PC, which means other tests such as digital rectal examination (DRE) are needed to confirm the disease [25]. PC is the most common type of cancer in men, especially in old age [4]. In the U.S., there are approximately 200,000 new cases of PC annually diagnosed and more than 30,000 men die every year from this disease [16]. Screening for PC by PSA at a young age is usually important for early diagnosis of this type of men's disease [17]. In addition to the 7.23 of incidence rates in men younger than 50 years in the United States, PSA screening identified more than one million men with PC especially in young men [26]. Among Arab men, the incidence of PC is very low [27]. Moreover, PSA screening has found that there is a 75% reduction in the proportion of men who have metastatic disease and 32.5% of the PC mortality rate through 2003 [28]. For a long time, PSA, which was approved for cancer detection by FDA in 1994, was considered the best marker for diagnosis of PC [28]. It plays an important role in invasion by PC cells [29]. However, the significant use of PSA as indicator for PC mainly depends on the age [30]. In older men, the sensitivity of PSA is very low to detect PC because the elevation level of PSA may result from many benign prostate diseases such as benign prostate type, sexually activity, urinary retention and prostatitis or from enlargement of prostate gland, while its sensitivity increases at younger ages [4, 15-17, 25]. Thus, usage of age-specific ranges are preferred to make PSA a more sensitive test in younger men than depending on normal value (4 ng/ml) [17, 28]. However, PSA is a specific marker for the prostate organ, but not for PC [16, 28].

Conclusion

Testicular cancer and prostate cancer were not detected in volunteer men. None of the men participating had elevated levels of all three biomarkers of testicular cancer. The PSA level was not high enough to predict the presence of prostate cancer (PC).

Conflicts of Interests

The authors have no conflict of interesting to disclose.

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