Serum And Bone Marrow Prostatic Speciafic Antigen And Prostatic Acid Phosphatase Levels In Patient's With Prostatic Cancer

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Abstract

Serum and bone marrow levels of prostatic specific antigen and prostatic acid phosphatase were analyzed and quantified by double antibody radioimmunoassay in 36 prostatic cancer patients, including 23 with metastatic cancer. There was a significant correlation between the serum and bone marrow levels of prostatic specific antigen and prostatic acid phosphatase independently of the metastases ($p < 0.001$). No patient with prostatic cancer and positive bone marrow prostatic specific antigen or prostatic acid phosphatase levels had normal serum levels. Quantification of bone marrow prostatic specific antigen and prostatic acid phosphatase does not provide more information than does serum determination.

Introduction

In 1990, many scientists introduced the importance of determining prostatic acid phosphatase levels in bone marrow to detect early metastatic prostatic cancer (1). Since that time, numerous reports have been published and no uniform criteria exist for usefulness of this tumor marker in the correct staging of the cancer. Between 1993 and 1997, some investigations, using enzymatic techniques, emphasized the prognostic value of the method and considered that an elevation in prostatic acid phosphatase indicates the existence of micrometastasis undetectable by other methods (2, 3). However, other investigations (4, 5, 6) found many false positive results in healthy subjects. Later, many workers (7, 8, 9)

compared the specificity of immunological and enzymatic methods, with the specificity of immunoassay and they found that after 3 years of

follow-up in 112 patients, 36% of those at high risk had metastases compared to only 3% of the remainders (10,11) .

In 1992, the serum and bone marrow prostatic acid phosphatase levels was determined simultaneously by radioimmunoassay and concluded that the level in bone marrow did not provide any additional information as did those obtained in serum (12, 13).

Because of these different results in the literature and the possibility to determine a new specific tumor marker of prostatic tissue (14), we compared serum and bone prostatic specific antigen and prostatic acid phosphatase levels for staging and prognosis in patients with prostatic cancer.

Materials and Methods

Prostatic specific antigen and prostatic acid phosphatase levels were determined in 36 patients with a histological diagnosis of prostatic cancer, and 34 control men with benign prostatic hyperplasia. The mean age of controls was 60 years (range 54-85 years) and that of the patients was 74 years (range 63-84 years). The stage was determined clinically and the patients have not received any treatment (2 have stage A, 3 stage B, 7 stage C and 24 stage D2 disease).

The bone marrow sample was obtained from the anterosuprior iliac crest and the serum sample was obtained simultaneously from the cubital vein with the patient under epidural anesthesia before transurethral resection. The samples were centrifuged for 15 minuets at 3000rpm and stored at -20 C^{o} . Prostatic specific antigen and ptostatic acid phosphatase levels were determined by double antibody radioimmunoassay (1), with a lower sensitivity limit of 0.2 ng / ml.

Statistical analysis was done with a statistical program of social science package program (SPSS), and the P value was obtained by the Mann-Whitney U test.

Results

In the control group the mean serum and bone marrow prostatic specific antigen levels was 5.2 ng/ ml. (rang 0.2-23 and 0.2-29.6, respectively). However, the mean serum prostatic acid phosphatase levels

was 1.6 ng / ml (rang 0.2-4.9), which was significantly lower than that in bone marrow (2.5 ng / ml, range 0.2-9.8, P <0.001). There was a significant correlation between the levels in serum and bone marrow for both tumor markers P <0.01 (Table 1).

We established 10 ng / ml, as the normal level of prostatic specific antigen in serum and bone marrow, and 2.5 and 6 ng / ml, respectively, as the normal levels of prostatic acid phosphatase. Similar qualitative levels of both markers were observed. Only 66 years – old patient with complicated benign prostatic hyperplasia had a normal serum concentration of prostatic specific antigen (5.8 ng / ml.) and a positive 4 level in bone marrow (15 ng / ml.) (Table 2).

A among the patients with prostatic cancer the serum prostatic specific antigen concentrations (mean 362.6 ng / ml. , range 0.2 to more than 1.000) were statistically similar to those in bone marrow (mean 377.9 ng / ml. , range 1.2 to more than 1.000) , as were the serum prostatic acid phosphatase concentrations (mean 79.3 ng / ml. ., rang 0.2 to more than 1000 and mean 85.6 ng / ml. , rang 0.2 to more than 1.000), respectively , (P <0.001) (Table 1).

The patients with osseous metastases show no significant difference between the levels of prostatic acid phosphatase and prostatic specific antigen in serum and bone marrow. However, they have higher levels of these markers than those without metastases (P <0.001). Finally, if one consider the qualitative relationship between both markers in serum and bone marrow, no patient had positive bone marrow and negative serum results (Table 2).

Discussion

Several studies have been done on the clinical usefulness of bone marrow prostatic acid phosphatase levels for early detection of bone metastases secondary to prostatic cancer. In this study, the level of prostatic acid phosphatase in the control group was superior in bone marrow than in serum. This difference was related to a cross- reaction with acid phosphatase of megakaryocytes and osteoblastic cells in bone

marrow (4, 6). Therefore, we established a higher normal level in bone marrow (6 ng / ml.) than in serum (2.5 ng /ml.) to avoid false positive results. However, this difference was not confined in the carcinoma group, in which both levels were high.

The results revealed a significant correlation between serum and bone marrow levels, which agrees with the findings of others (12, 15. 16). By qualitative analysis no patients with positive bone marrow samples had negative serum sample. Therefore, the bone marrow samples did not provide any additional information as obtained with serum.

We considered the importance of proststic specific antigen in bone marrow because there are no cross-reaction with acid phosphatase and no other sources of prostatic specific antigen in bone marrow. Therefore, a higher level in bone marrow would signify bone metastases. The results have confirmed that prostatic specific antigen concentrations in serum and bone marrow are the same in the controls and in patients with prostatic cancer with or without metastases, with an excellent correlation between the groups. We conclude that the quantification of prostatic specific antigen and prostatic acid phosphatase in bone marrow correlates with that in serum, without providing any additional information. This finding is explained anatomically and physiologically by the fact that the bone marrow is drained continuously by the lymphatic system and blood circulation, and it does not exist as a separate entirely since it is in close contact with the rest of the bodily circulation

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Table(1): Serum and bone marrow prostatic specific antigen and Prostatic acid phosphatase levels

Item	Controls	Patient with Cancer		
		With Metastases	Without Metastases	Totals
Number of Patients	34	23	13	36
Prostatic specific antigen (ng/ml)*				
Serum	5.2±5.9	455.7±344.3	170.3±237.5	362.6±334.7
Bone Marrow	5.2±6.0	492.2±359.0	165.6±237.5	377.9±35102
Prostatic acid phosphatase (ng / ml)*				
Serum	1.6±1.3	115.7±281.8	14.9±34.9	79.3±229.6
Bone Marrow	2.5±1.4	124.0±280.9	16.8±38.7	85.6±229.9

***Mean ± Standard error**

Table (2): Qualitative relationship between serum and bone marrow proststic specific antigen and prostatic acid phosphatase levels

Marker	Qualitative relationship (serum/ bone marrow)			
	Positive/ Positive	Positive/ Negative	Negative/ Positive	Negative/ Negative
Controls (34 patients) Prostatic specific antigen	6	2	1*	25
Prostatic acid phosphatase	2	3	0	29
With cancer (36 patients) prostatic specific antigen	33	0	0	3
Prostatic Acid phosphatase	24	2	0	10

***Benign prostatic hyperplasia – serum 5.8 and bone marrow 11.1 ng / ml.**

مستويات المستضد النوعي البروستاتي والفوسفاتيز الحمضي البروستاتي في مصل ونخاع العظم للمرضى المصابين بسرطان البروستات

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الخلاصة

تم تحديد وقياس مستويات المستضد النوعي البروستاتي والفوسفاتيز الحمضي البروستاتي في كل من المصل ونخاع العظم بواسطة القياس الإشعاعي المناعي مزدوج الضد في 36 مريض بسرطان البروستات ، من ضمنهم 23 مريض بالسرطان المنتشر . وجد أن هناك ارتباط معنوي بين المستويات المصلية ومستويات نخاع العظم ، بغض النظر عن انتشار المرض باحتمالية اقل من 0.001 ($0.001<p$) .

كما لوحظ عدم وجود مستويات ضمن المستوى الطبيعي للمستضد النوعي البروستاتي والفوسفاتيز الحمضي البروستاتي في المرضى المصابين بسرطان البروستات سواء في المصل أو في نخاع العظم. أثبتت الدراسة ، بان القياس الكمي لكل من المستضد النوعي البروستاتي والفوسفاتيز الحمضي البروستاتي في نخاع العظم لم تعطينا معلومات أكثر من تلك التي حدّدت في المصل.