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PROSTATE-SPECIFIC ANTIGEN LEVELS IN ACUTE AND CHRONIC BACTERIAL PROSTATITIS

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Prostate-specific antigen (PSA) is now widely accepted as a useful tumor marker for the diagnosis and follow-up of prostatic cancer. An elevated level of PSA has been asserted to be highly specific for prostate cancer, although patients with large benign prostate glands and those with bacterial prostatitis may also have slightly elevated levels. We measured the serum PSA level in the patients with acute and chronic bacterial prostatitis and consecutively monitored the PSA level in 6 patients who had acute prostatitis and an elevated PSA level. The PSA level was found to be elevated during the acute phase of prostatic inflammation, and the elevated, PSA level in the patients with acute prostatitis returned to the normal level within 14 days after initiation of antimicrobial therapy in all 6 patients. In one patient with chronic prostatitis the elevated PSA level persisted after antibiotic treatment. He was found to have adenocarcinoma by transrectal ultrasonography and biopsy. A markedly elevated serum PSA level in bacterial prostatitis can cause confusion in the diagnosis of prostatic carcinoma. Therefore, PSA determination should be obtained after complete clinical resolution of inflammation to exclude prostatic malignant involvement.

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Key words: Prostate-specific antigen, Bacterial prostatitis

INTRODUCTION

Since the determination of the serum prostate-specific antigen (PSA) is now in wide use in the diagnosis[1-3], staging[3,4], and management[4,5] of patients with prostatic adenocarcinoma, it is important to define the conditions which cause its elevation. PSA is a serine protease originally isolated from prostatic tissue by Wang and associates[6] in 1979. This unique glycoprotein is specific for and produced by all types of prostatic epithelial tissue. In addition to adenocarcinoma of the prostate, many non-malignant conditions such as benign prostatic hyperplasia, acute and chronic prostatitis, and prostatic infarction can increase the serum PSA concentration[7]. Prostatic intraepithelial neoplasia, presumed to be a premalignant disorder, also has been associated with a slight elevation in the serum PSA level[8]. Additionally, instrumentations, such as cystoscopy and selected manipulations of the prostate (namely, prostatic massage and biopsy), can transiently increase the serum PSA value.

The exact extent of these changes in the serum PSA concentration is still under investigation.[9,10]. Histopathological examination revealed the presence of prostatitis in up to 75% of prostatic cancer specimens[11], and this condition may cause confusion in the diagnosis and management of prostate cancer using the PSA value. We investigated the serum PSA level in the patients with acute and chronic bacterial prostatitis. Furthermore, we monitored the PSA level chronologically in the patients with acute bacterial prostatitis and elevated serum PSA, level.

PATIENTS AND METHODS

Twenty men, between 28 and 75 years old, were seen in our clinic with signs and symptoms of prostatitis. Of the 20 patients, 10 had acute bacterial prostatitis, irritative voiding symptoms of dysuria, frequency and urgency, with sudden onset of moderate to high fever, chills, and perineal pain. The remaining 10 patients who had symptoms of prostatitis were diagnosed as having chronic bacterial prostatitis. They had bacteriuria caused by the same bacte-

rial species that were localized in the prostate. Prostatic inflammation was defined as >10 leukocytes per high-power field (hpf) (×400) of prostatic secretions[12]. Bacteria were considered to be localized in the prostate if there was at least a 10-fold increase in CFU per milliliter between the first-void urine (VB1) specimen and the postmassage urine (VB3) specimen or the expressed prostatic secretions (EPS) if the VB3 specimen did not meet this criterion[13]. Serum for determination of PSA levels was drawn prior to digital rectal examination and the patients received 1~3 months of treatment with trimethoprim-sulfamethoxazole. After disappearance of infection as determined by urine culture, the leukocyte count of the expressed prostatic secretions, and symptoms, the PSA levels were repeated in cases of initially elevated PSA level. The patients with acute prostatitis and elevated serum PSA level were followed with PSA determination weekly for 1 month. All patients who did not have a PSA <4.0 ng/ml by that time underwent transrectal ultrasonography and biopsy of any suspicious areas. The serum PSA levels were measured by the commercial EIA assay (Markit FPA, Dainippon Pharmaceutical Co., Ltd.) and the normal reference range was 0 to 3.6 ng/ml. PSA values were analyzed by using Wilcoxon rank-sum test for differences between acute and chronic prostatitis groups.

RESULTS

Table 1 shows the clinical features and PSA levels in the patients with acute and chronic bacterial prostatitis. All patients were treated for 2~12 weeks, depending on the leukocyte count of the expressed prostatic secretions. The serum PSA levels in the patients with acute bacterial prostatitis was 0.5~21 ng/ml (mean 8.3 g/ml) on initial presentation. Of the 10 patients with acute bacterial prostatitis 6 had an eleva ted serum PSA level before treatment, which returned to the normal level within 14 days after initiation of antibacterial therapy in all patients. Table 2 shows the PSA values for the 6 patients with acute bacterial prostatitis before and after treatment. The recognized uropathogens in the cases of acute bacterial prostatitis included

Table 1. Clinical features and PSA values in the patients with bacterial prostatitis

Patient	Age	Type of Prostatitis	PSA (ng/ml)	Organism
1	44	acute	4.2	E. coli
2	35	acute	1.9	E. coli
3	29	acute	0.5	Klebsiella pneumoniae
4	51	acute	8.2	E. coli
5	68	acute	21.0	E. coli
6	54	acute	16.0	Proteus mirabilis
7	63	acute	9.1	Pseudomonas aeruginosa
8	49	acute	18.0	E. coli
9	72	acute	2.2	Diphtheroids
10	62	acute	2.1	E. coli
11	77	chronic	1.5	Proteus mirabilis
12	66	chronic	2.5	E. coli
13	72	chronic	7.1	E. coli
14	60	chronic	1.0	Coagulase-negative-staphylococci
15	23	chronic	0.5	Pseudomonas aeruginosa
16	71	chronic	1.4	E. coli
17	68	chronic	2.6	E. coli
18	33	chronic	1.0	Enterococcus faecium
19	38	chronic	1.4	Alpha-hemolytic streptococci
20	57	chronic	3.5	Enterobacter cloacae

Table 2. PSA values (ng/ml) before and after treatment of acute prostatitis with antimicrobial agent

Case	Before Treatment	Day 7	Day 14	Day 21	Day 28
1	4.2	1.5	1.5	2.1	1.7
4	8.2	2.2	1.6	1.7	1.5
5	21.0	5.8	2.1	1.8	1.5
6	16.0	4.0	1.5	2.1	1.8
7	9.1	2.6	1.7	1.5	1.5
8	18.0	4.5	1.8	1.6	1.7

Escherichia coli in 6 cases, and *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Diphtheroids* in 1 case each.

The serum PSA level in the patients with chronic bacterial prostatitis was 0.5~7.1 ng/ml (mean 2.3 ng/ml) on initial presentation. All but 1 patient with chronic bacterial prostatitis had a normal serum PSA level (Table 1). In this patient, the elevated PSA level persisted after completion of the course of antimicrobial therapy and underwent transrectal ultrasonography of the prostate with multiple biopsies, and then was found to have adenocarcinoma. The causative organisms of chronic prostatitis consisted of *E. coli* in 4 cases, and *P. mirabilis*, coagulase-negative *Staphylococci*, *P. aeruginosa*, *Enterococcus faecium*, alpha-hemolytic *Streptococci*, and *Enterobacter cloacae* in 1 case each.

The serum PSA values in the patients with acute prostatitis were significantly higher than those in the patients with chronic prostatitis ($p<0.05$).

DISCUSSION

Since its discovery by Wang et al.[6], PSA (a glycoprotein with a molecular weight of 33 kD) has been used widely for the staging and management of patients with prostatic cancer. PSA is produced exclusively by the epithelial cells that line the acini and ducts of the prostate gland; any condition that disrupts the cell-to-cell architecture within these acini and ducts can allow the PSA to "leak" into the prostatic parenchyma. Then, PSA enters the lymphatic and capillary system and increases the serum PSA concentration. Adenocarcinoma of the prostate gland often causes such a prostatic change and concomitantly increases the serum PSA value. Many common nonmalignant prostatic diseases also can disrupt this cell-to-cell architecture and cause a sustained increase in the serum PSA concentration.

Prostatitis, both acute and chronic, also has been shown to increase the serum PSA value. Recently, there have been several reports of elevation of PSA in acute and chronic bacterial prostatitis. In a study of 30 men with chronic prostatitis, Robles and co-workers[14] found that the serum PSA level ranged from 0.2 to 11.8 ng/ml (mean±SD, 2.88±3.24 ng/ml). In 50 men with acute prostatitis, these same authors noted that the serum PSA concentration ranged from 0.2 to 124 ng/ml (mean±SD, 18.09±33.01 ng/ml). Morote et al. showed elevation of PSA in 24% of the patients with acute prostatitis and 3.3% of those with chronic prostatitis in a total of 1,383 patients[15]. These findings suggest that elevation of the PSA level is associated more frequently with acute prostatitis. Studies in which the serum PSA level is monitored every week after treatment in the patients with acute bacterial prostatitis have not been reported. Elevated PSA levels in patients with acute bacterial prostatitis returned to the normal level within 14 days after appropriate antimicrobial therapy. Therefore, the serum PSA should not be determined during the acute phase of prostatitis. After clinical resolution of prostatitis a more relevant and useful PSA value can be obtained to exclude prostatic malignancy.

The mechanism by which the PSA level is elevated in prostatitis is not clear. Prostatic acinar cell disruption, with subsequent leakage of the antigen during the acute inflammatory process, has been sugges ted as an underlying mechanism. The extracellularly released PSA was shown to be transported by neutrophils and macrophages from the prostate stroma to the serum as a result of increased vascularity of the prostate gland at the time of the acute inflammatory process. This is consistent with the findings obtained by immunohistochemical studies which showed confine-

ment of PSA to the cytoplasm of prostatic acinar cells and ductal epithelium[16]. An ultrastructural study of the localization of PSA in benign and malignant prostatic tisseus[17] has shown that PSA is localized within the endoplasmic reticulum, cytoplasmic vesicles and vacuoles, and the lumen of prostate glands. Consequently, any pathological process which causes prostatic cellular destruction can lead to an elevation in the serum PSA level. A traumatic leak phenomenon is considered to be the cause of sustained elevation in serum PSA level after prostatic biopsy[18].

In conclusion, the association between acute prostatitis and elevated PSA level may be attributed to the disruption of the prostatic acinar cells resulting in leakage of the antigen into the serum. The elevated PSA level during the acute phase of prostatic inflammation returned to the normal level within 14 days after initiation of proper antibacterial therapy in all cases. Therefore in the patients with prostatitis PSA determination should be repeated after clinical resolution of prostatitis to exclude prostatic malignancy.

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和文抄録

急性および慢性前立腺炎における前立腺特異抗原の検討

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前立腺特異抗原（PSA）は，前立腺癌の診断および経過観察に有用な腫瘍マーカーとして現在広く用いられている．前立腺特異抗原の上昇は前立腺癌の存在を強く示唆するものであるが，同様の現象は高度の前立腺肥大症や前立腺炎においても認められる．今回われわれは，急性および慢性前立腺炎患者の PSA を測定し，さらに PSA の上昇が認められる6例の急性前立腺炎患者における，PSA の経時的変化の検討を試みた．PSA は炎症の急性期に上昇する傾向が有り，適切な抗菌剤の使用により全例14日以内に正常化した．慢性前立腺炎患者に治療後もなお PSA が正常化しない症例が1例あり，経直腸的超音波検査と生検により前立腺癌と診断された．従って，前立腺癌を除外するためには，炎症が完全に消退したのちに再び PSA を測定すべきである，

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