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Original Article

Serum Prostate-specific Antigen Following Antibiotics in Symptomatic Patients with Lower Urinary Tract Symptoms

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Abstract

Introduction: With the current practice of routine Serum PSA examination, there arises a diagnostic dilemma with regard to their further evaluation and treatment.

Aim: The aim is to study the incidence of cancer (CA) prostate in cases with elevated Serum PSA.

Methodology: We studied 50 men aged between 50 and 80 years with elevations in Serum PSA (total PSA) after certain exclusion criteria, these cases are given a course of antibiotics for 6 weeks and repeat Serum PSA levels obtained. In those with persistent elevation in Serum PSA above 4 ng/ml, transrectal ultrasound-guided biopsy was done.

Results: In our study population, 36.6% of cases with persistent PSA elevation were proven positive for malignancy by biopsy.

Conclusion: A fall in Serum PSA following a course of antibiotic therapy does not exclude the presence of a carcinomatous element in prostates.

Key words: Serum prostate-specific antigen, Antibiotics, Lower urinary tract symptoms

INTRODUCTION

Incorporation of prostate-specific antigen (PSA) into clinical practice has revolutionized the diagnosis and treatment of patients with prostate cancer (CA); it has become the most useful tumor marker in this neoplasm.[1] It is, however, an organ-specific and not pathological marker and significant overlap is found in its concentrations in patients with benign hyperplasia (BPH), prostatitis, and clinically localized CA. Although the clinical criterion for prostate biopsy is established at a PSA cutoff level of 4 ng/mL, approximately 80% of biopsies fail to confirm the presence of CA when the cutoff is below 10 ng/mL.[2] A cutoff level of 25 ng/ml may detect 95% of CAs, thereby avoiding approximately 20–25% of unnecessary biopsies.[3,4] Both BPH and prostatitis are known causes of raised PSA.[5,6] 25% of patients with a histological diagnosis of BPH and up to 70% with a clinical diagnosis of acute prostatitis present PSA concentrations above the cutoff. However, controversy exists as to the influence of subclinical inflammatory foci on the elevation of the marker.[7] Histological prostatitis is a frequent finding in biopsies of patients with no clinical evidence of prostatitis, and a variable relationship with PSA concentration has been reported. For some authors, the influence of inflammation would be related not to the extension of foci but to their intensity and the degree of epithelial disruption, while, for others, it would depend more on the type of inflammation.

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Aim

The aim is to study the incidence of CA prostate in cases with lower urinary tract symptoms with elevated Serum PSA.

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METHODOLOGY

In this prospective study, 50 men of age between 50 and 80 years who presented with lower urinary tract symptoms with elevated Serum PSA to the outpatient department were included.

We excluded the following criteria: Acute urinary retention, catheterization within 48 h, urinary tract infection, UB calculi, prostatic abscess, recent prostate biopsy, large volume BPH – >60 CC, nodular prostate in digital rectal examination (DRE), and obvious CA prostate in DRE.

At the time of examination, only patients with non-suspicious DRE and a Serum PSA concentration between 4 and 20 ng/mL were analyzed.

Elevations in Serum PSA (total PSA) ranged from 6 ng/ml to 20 ng/ml.

DRE findings: Firm to Very Firm in consistency.

Ultrasound imaging (USG) abdomen: Radiologists reported the volume of prostate, obvious variations in echogenicity.

Urine C/S-based antibiotic was given for an average of 10 days, following which they received a course of broad-spectrum antibiotic for 6 weeks. Antibiotic was given singly or in combination - one antibiotic for 3 weeks followed by another for the next 3 weeks. For all cases, tablet tinidazole 500 mg BD was given for 3–6 days, for anaerobic coverage. Analgesics and gut protective (tablet lactic acid bacilli and tablet rabeprazole) were given. Broad-spectrum antibiotics used in our study are tablet ciprofloxacin 500 mg BD and tablet cotrimoxazole 2 BD along with two doses per week of 3 g fosfomycin, capsule doxycycline 100 mg BD, and tablet faropenem ER 300 mg BD. Following antibiotic therapy for 6 weeks, cases were evaluated for the following – Symptomatic relief, post-void residual urine volume measurements using USG, Serum PSA, repeat DRE, and urine C/S.

RESULTS

Irrespective of pre-treatment PSA levels, of 50 cases studied, 20 cases Serum PSA fell <4 ng/ml, 18 cases Serum PSA fell to levels between 6 and 10 ng/ml, 8 cases marginal

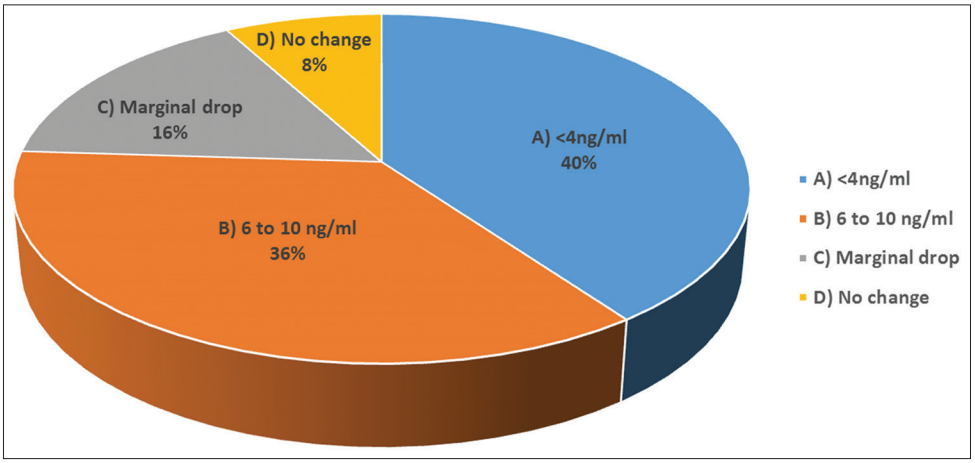

Figure 1: Serum prostate-specific antigen levels following 6 weeks of antibiotics

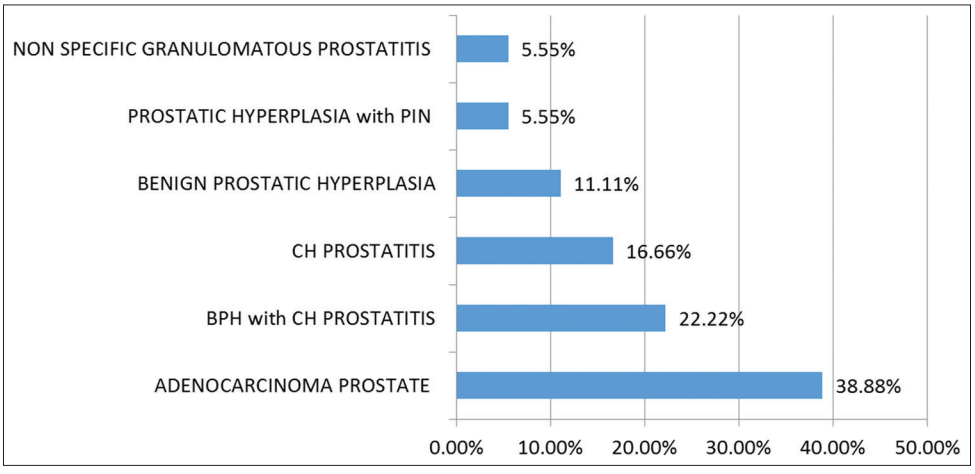

Figure 2: Out of 18 cases with fall in serum prostate-specific antigen to between 6 and 10 ng/ml-histopathology

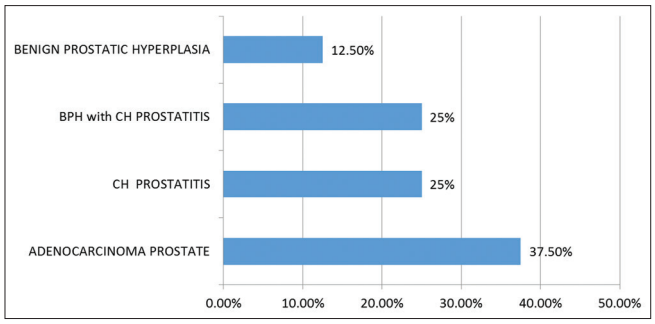

Figure 3: Out of 8 cases with marginal drop in serum prostate-specific antigen by 1–2 ng/ml-histopathology

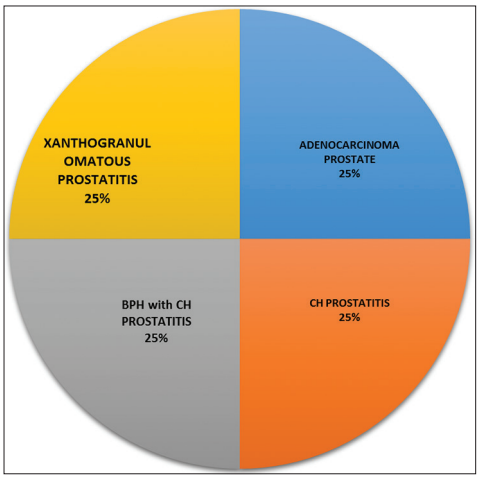

Figure 4: Out of 4 cases with nil change in serum prostate-specific antigen levels-histopathology

drop in Serum PSA level by 1–2 ng/ml, 4 cases no change in Serum PSA level [Figure 1].

The 20 cases (a) were put under surveillance, yearly DRE and SPSA. Of these 20 cases, 7 of them defaulted. The rest are yet to show alterations in DRE or PSA levels.

Rest of the 30 cases underwent transrectal ultrasound (TRUS)-guided prostate biopsy – six quadrants/altered echo-directed biopsies. Haptoglobin-related protein (HPR) reports of them are provided below.

Of the 18 cases (b), 7 cases were reported adenocarcinoma prostate, 4 cases were reported BPH with CH prostatitis, 3 cases were reported CH prostatitis, 2 cases were reported BPH, 1 case was reported BPH with a prostatic intraepithelial neoplasia, and 1 case was reported non-specific granulomatous prostatitis [Figure 2].

Of the 8 cases (C), 3 cases had adenocarcinoma prostate, 2 cases had CH prostatitis, 2 cases had BPH with CH prostatitis, and 1 case had BPH [Figure 3].

Of the 4 cases (D), 1 case was reported adenocarcinoma prostate, 1 case was reported CH prostatitis, 1 case was reported BPH with CH prostatitis, and 1 case was reported xanthogranulomatous prostatitis [Figure 4].

In category B, 7 of 18 cases have HPR proved adenocarcinoma [38.8%], [C] 3 of 8 cases HPR-proven adenocarcinoma [37.5%], and [D] 1 of 4 cases HPR -proven adenocarcinoma [25%]. Of 30 cases with persistent elevation in PSA (B+C+D), 11 cases (36.7%) were HPR-proven CA prostate by TRUS-guided biopsy.

DISCUSSION

Prostate CA is determined in only 34% of biopsies performed on the basis of PSA elevation[8] and in 20–30% in patients with normal DRE and PSA values of between 4 and 10 ng/mL. Therefore, there is a high level of unnecessary biopsies, particularly in this group.[9] The literature demonstrates a relationship between acute and chronic inflammations with elevated PSA, but there have been recent studies that suggest the effects and benefits of chronic prostatitis treatment on PSA.[10,11]

Okada *et al.*[12] and Schatteman *et al.*[7] concluded that subclinical inflammation could cause PSA elevation and emphasized the fact that nearly half of all clinically asymptomatic men with elevated PSA levels have laboratory signs of prostatitis. They suggest that the use of antibiotics would result in a decrease in PSA levels in almost 50% of patients, thereby avoiding BxP. This approach, however, requires careful follow-up, especially for patients whose PSA levels fail to decrease to within the normal range. Kaygisiz *et al.*[1] and Del Rosso *et al.*[11] suggested that AT should be administered for 3 weeks, regardless of the presence of inflammation when PSA levels are in the gray zone, before making a decision regarding whether or not to carry out a biopsy.

Hochreiter *et al.*[13] showed a PSA reduction in 63% of patients following AT, with PSA returning to normal values in 9% of cases, thus avoiding prostate biopsy. After AT, Potts.[14] documented PSA normalization in 42% of patients, and Carver *et al.* found the same in 41% of patients. These studies did not perform BxP in all patients to exclude the diagnosis of PCa after treatment.[15]

The influence of prostatitis on PSA concentrations remains a controversial issue.[16] Ozen *et al.*[17] claimed that BPH and prostatitis appear to be more frequent causes of PSA elevation. Scardino[18] recommended that asymptomatic men presenting with a modestly elevated PSA level (<10 ng/mL) and a normal digital rectal examination could be reassured, and then, the PSA level could be repeated once or twice; if the levels remained elevated, this would

be an indication of the need to perform a biopsy. Stopiglia *et al.*,[19] in a prospective randomized and double-blind trial with placebo, demonstrated that PSA reduction occurred after antibiotic and placebo application and suggested that a decrease in PSA does not indicate the absence of PCa. Recently, Faydaci *et al.*[20] demonstrated that AT given to patients with PSA levels higher than the threshold value has not led to a significant change in prostate needle biopsy decisions and suggested that BxP should be considered without the use of AT in patients with high PSA values if suspicion of prostatitis does not exist.

CONCLUSION

Fall in Serum PSA levels following rigorous antibiotic therapy does not exclude the presence of a carcinomatous element in prostates. In the current era, with the advent of laparoscopic radical prostatectomy & Advanced radiotherapy modalities, it is SAFER to subject ALL cases with elevated S.PSA, irrespective of DRE findings, to TRUS guided biopsy for early detection of CA prostate.

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