CLINICAL SIGNIFICANCE OF SERUM PSA (PROSTATE SPECIFIC ANTIGEN) IN TREATMENT OF PROSTATE CANCER

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Abstract- Prostate specific antigen (PSA) has been described as a single test with highest positive predictive value for diagnosing carcinoma of prostate. Routine use of PSA helps in diagnosing organ-confined prostate cancers.

Monitoring the evolution of prostate cancer has crucial importance since this tip of neoplasia has a variable biology, ranging from latent cancers to extremely aggressive tumors. At the moment, PSA (prostate specific antigen) values point out to either successful or unsuccessful prostate cancer therapy. Depending on therapeutic strategies, biochemical recurrence (BCR) is differently defined.

During 20 years (1994 and 2013), 66130 patients were screened for various tumour markers. PSA screening was done in 36152 including clinical BPH which amounts to 54.66 %. Majority (78.53%) showed normal values, 8.05% had cancer while 13.42% with hypertrophy. Percentage of false positive and false negative was 0.67%. Initial assessment included the International Prostatic Symptom Score, and the quality of life index, digital rectal examination, urinalysis, prostate specific antigen, uro-flow and residual urine estimation. In this study, some interesting cases were discussed. Our findings show that though PSA helps in diagnosing malignancy, it was found that single observation of high values was not indicative of malignancy, however, serial detection with help of biopsies revealed the existence of hypertrophy or bacterial prostatitis.

Keywords- Prostate cancer, Prostate Specific Antigen, Surgery, Serial estimation

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Introduction

Prostate cancer is the second most common malignancy in men globally. It is known to have increased prevalence with advancing age. Prostate Cancer is the most commonly diagnosed visceral cancer in USA and other parts of the world including India. At Mumbai registry, the age adjusted incidence rate was 5.2/100,000 and it ranked 8th in initial period, while at the end of study period there was an 20% increase in age adjusted incidence rate (6.3/100,000) and occupied 4th rank in leading site [1].

Prostate specific antigen (PSA) is a glycoprotein, produced in high levels by epithelial cells of the prostate gland in men and very little amount is leaked into the blood, due to the presence of basement membrane under normal condition. Wang and co-workers in 1979 purified a protein from prostate tissue and named it Prostate specific antigen [2].

PSA has been described as a single test with highest positive predictive value for diagnosing carcinoma of prostate [3]. However, the role of PSA in screening remains controversial [4-7].

In addition, PSA is used as an indicator of progression or clinical response after treatment for prostate cancer, but the prognostic value of this marker is limited. Current studies are evaluating a number of alternative markers, such as PSA-related parameters,

human kallikrein 2, osteoprotegerin and the gene DD3 (PCA3), that may improve the specificity of current PSA-based diagnostics and the prognostic value of PSA [8]. A few interesting cases were discussed in the present study.

Methods

Eight thousand patients with clinical BPH, prostatitis and other prostate complaints were received and tested for PSA investigation between 1994 and July 2013. As far as Ethic approval is concerned, these cases were referred to our Laboratory by various Clinicians of the Hospital Bombay (indoor/OPD). The Lab was not directly involved with patients. These cases come for required investigation with referring Doctor's note and clinical history. Hence, Ethical approval is not specified in the present study and consent form was not required.

Initial assessment included the International Prostatic Symptom Score, and the quality of life index, digital rectal examination, urinalysis, prostate specific antigen, uro-flow and residual urine estimation. Patients were then divided into: Stage 1, those with no bothersome symptoms and no significant obstruction, they can generally be watched. Stage 2, those with bothersome symptoms but without significant obstruction, they can be treated with pharmacotherapy/ thermotherapy. Stage 3, those with significant obstruction defined

as uro-flow of less than 10 ml/s with persistent residual urine of > 100 ml, transurethral prostatic resection (TURP) would be recommended. Stage 4, those with complications of BPH such as chronic retention of urine and bladder stone, they would need TURP. Serum PSA level was detected using Abbotts Axsym and Roche Elecsys analyzers.

Prostate cancer was confirmed by PSA estimation in conjuncture with ultra sound, CT, MRI and biopsy. The serial PSA levels were carried out before and after surgery and chemotherapy. Decreasing trends in serum PSA level (values) was observed to assess the status of the disease.

Study of monitoring of serum PSA level in various stages of disease was found to be useful especially in post surgery during and after chemotherapy and recurrence of disease. It was also found useful in detection of benign state of hyperplasia of prostate, prostatitis in conjuncture with biopsy and medication.

Three interesting cases of prostate cancer were discussed in the present study to find usefulness of estimation of serum PSA.

Case 1

A 53 year man presented himself with chief complaints of sweating for 6 months, increased frequency of micturition day and night (D/N) was 30-40 mints/ 2-3 times, poor stream, hesitancy for 5-6 months and had chest pain for 15 days. The initial serum PSA level was 194 ng/ml. Biopsy confirmed poorly differentiated adenocarcinoma of prostate (cell pattern invasive cords and ill formed small acini lined by cuboidal cells with irregular hyperchromatic nuclei) with a Gleason sum of 9. He underwent orchidectomy, and reported for all four post operative follow-up. His post operative follow-up PSA levels were 0.00, 0.01, 0.06 and 0.00 ng/ml respectively. Present status-The patient is doing well. The above case showed the importance of the study of PSA in the follow-up of patients undergoing surgery [Fig-1].
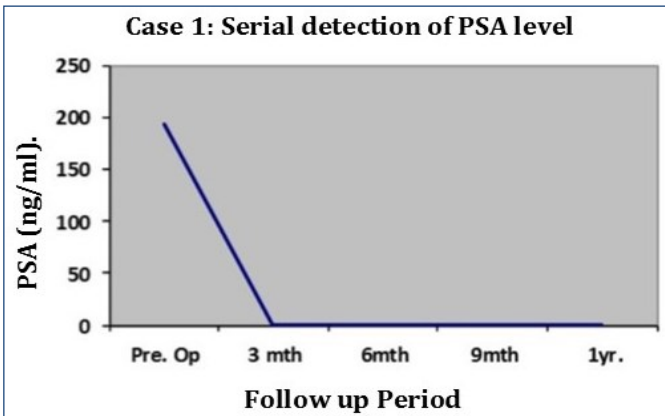

Fig. 1- Case 1: Serial detection of PSA level

Case 2

A 59 year man came with complaints of nocturia, burning micturition, urgency and post void dribbling since 2 months. The initial serum PSA level was 23.22ng/ml. biopsy confirmed moderately differentiated adenocarcinoma of the prostate. He underwent radical prostatectomy and was regular for all follow ups. During his first post operative follow-up, the PSA level was 8.85ng/ml, then on the second follow-up it elevated to 16.18ng/ml; at this stage he received treatment of decapeptyl-depot a (GnRH)-1 injection per month. During his third and fourth follow-up, the PSA levels dropped sharply to 1.62ng/ml and 0.06ng/ml respectively. Present status-The

patient is doing well. The above case showed the advantage of PSA levels study in monitoring the response to therapy [Fig-2].
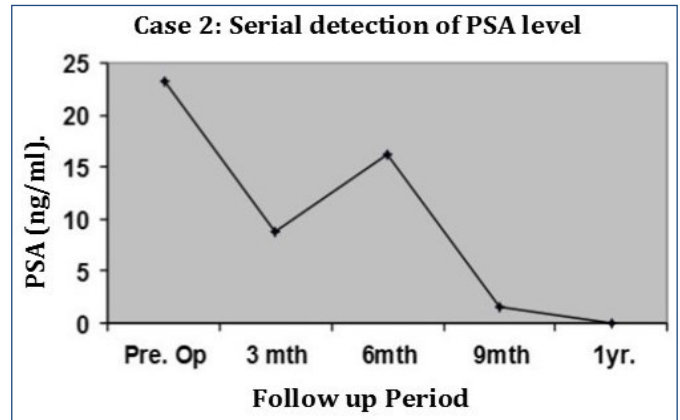

Fig. 2- Case 2: Serial detection of PSA level

Case 3

A 68 year man came with complaints of low back ache and poor stream since 10 days. The initial serum PSA level was 144ng/ml. A prostate needle biopsy confirmed a poorly differentiated adenocarcinoma of the prostate (cell pattern ill defined acinar structures and cords of oval to cuboidal cell with hyperchromatic nuclei) with a Gleason sum of 8. He underwent orchidectomy. His first post operative follow-up PSA level was 23ng/ml, the second follow-up PSA level was 12.9ng/ml and of the third follow-up was 103ng/ml. During this period he was admitted for loss of appetite, weakness, Urinary tract infection (UTI) and severe right leg lymph-oedema. His DRE revealed a flat gland. Has a positive [Fig-3].
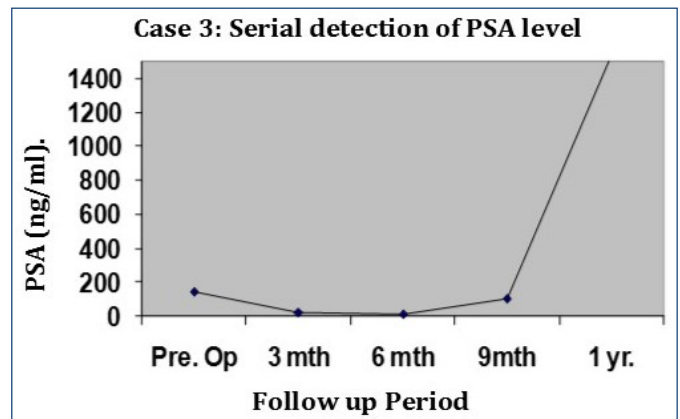

Fig. 3- Case 3: Serial detection of PSA level

Discussion

Estimation of serum PSA is a useful tool for diagnosis of prostate cancer. The Serial measurement of serum PSA levels, during the treatment and follow up of one year, guided to determine the response to therapy and monitor disease regression as seen in case no 2 of the present study. Similar findings were reported by Arai, et al. and Matman, et al. [9,10].

In the present study, multidisciplinary approach was applied using digital rectal examination (DRE) Digital rectal examination. A routine screening test that is used to detect any lumps in the prostate gland or any hardening or other abnormality of the prostate tissue., ultrasound, CT, MRI, biopsy and serial estimation of PSA. Malati, et.al. used various parameters including PSA for detection of prostate cancer [11], however, author did not specify the exact role of PSA.

In this study, the value of PSA was found decreased in serial estimation of PSA levels during one year follow up. Montie, et al. and Stamey, et al. [12,13] described 3 cases with 9 year follow up and reported importance of PSA in establishing the diagnosis of metastatic stage of prostatic cancer and also provided information on the course of the disease and response to treatment.

Myrtle, et al. [14], Staney, et al. [15] and Gutha, et al. [16] had reported a correlation between clinical stages and PSA levels. The PSA level increased with higher clinical stages of disease. Elevated PSA levels showed progressively increased cancer stages from A to D. In our study, it was seen that as pathological stages(using Gleason score) advances serum PSA level also increased and decreased after treatment (Case no 2).

In the third case patient underwent orchidectomy. The first and second follow up showed considerable decrease in level of PSA. However, patient developed urinary tract infection and subsequently PSA level shot up.

Patients diagnosed by annual prostate cancer screening appeared more likely to experience an indolent PSA recurrence and less likely to die of prostate cancer after PSA recurrence compared with patients referred from the community [17].

Conclusion

Though PSA estimation has been controversial test, however, it plays an important role during monitoring of schedule treatment. Prostate-specific antigen-based serial screening may decrease prostate cancer-specific mortality.

Acknowledgements

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