Retrospective Study of Prostatic Disease in a Regional Hospital and Re-Evaluation of Acid Phosphatase as a Marker for Prostatic Carcinoma

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Summary

A 5 year retrospective study was carried out to evaluate the number of patients with prostatic cancer dealt with in a Regional unit and to reevaluate the efficacy of serum acid phosphatase as a diagnostic tool. The results showed that out of 319 patients 16.3% had malignant prostates but only 17.31% of these had a raised serum acid phosphatase level. The majority (86.79%) of the patients had a transurethral procedure.

Introduction

During a 5 year period from May 1982 to April 1987, 419 prostatectomies were performed in the Regional urology unit in the county of Limerick with a population of about 300,000. The majority of procedures were performed by the senior author. Out of these, complete records were retrieved for only 319 patients and only these have been considered for this study. The study was initially started to evaluate the results of acid phosphatase when the histological diagnosis was available and to identify the reasons for the false positive and negative results and whether we could improve by taking specific fault rectifying steps. We also carried out an audit of the number and age group of the patients suffering from prostatic disease undergoing surgery, the number having carcinoma and the type of procedures performed.

Aims of the study

1. To identify the number of prostatic cancer patients in a

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A retrospective study from May 1982 to April 1987 in a random population attending with prostatic disease to a Regional urology unit in Ireland.

2. To identify the age group undergoing prostatectomy.

3. To identify the type of operation performed.

4. To re-evaluate the efficacy of serum acid phosphatase as a marker for the most common male malignancy and to query the need to change to an investigation with better diagnostic accuracy.

Results

The results of this retrospective study were obtained from the records of 319 patients. The presentation was broadly divided into those with

a) prostatism = 203 - 63.64%
b) retention = 116 - 36.3%

Total no. of benign prostatic hypertrophy = 267 - 83.7%
Total no. of malignant prostates = 52 - 16.3%

Clinically 14 patients were thought to have prostatic carcinoma with two false positives. In addition 5 patients were known to have prostatic carcinoma at admission.

Histological breakdown of malignant prostates:

Focus of adenocarcinoma = 3
Moderate to well diff. adenocarcinoma = 38
Poorly diff. carcinoma = 6
Undiff. carcinoma = 4
Lymphocytic lymphoma = 1

Procedures performed: 318

1. Transurethral prostatic procedures = 276 86.79%
   1a. Transurethral resection of prostate = 259
   1b. Transurethral resection of bladder neck = 11
   1c. Transurethral prostatic incision = 6
2. Open prostatectomies = 42 13.21%
   2a. Transvesical = 13
   2b. Millin's = 16
   2c. Vescicocapsular = 13

3. Associated procedures:
   Dorsal slit = 7
   Cystolitholapexy = 4
   Transurethral resection of bladder tumours = 2
   Prostatic calculi removal = 3
   External meatoctomy = 2
   Circumcision = 1
   Bilateral subcapsular orchidectomy = 5

All patients undergoing a transurethral procedure had an internal urethrotomy.

Serum acid phosphatase levels

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\begin{align*}
&\text{\(\leq 11\) were} & = & 294 & 92.16\% & \text{(normal range)} \\
&\text{False positive} & = & 27 & 9.18\% \\
&\text{True positive} & = & 267 & 90.82\% \\
&\text{> 11 were} & = & 25 & 7.84\% & \text{(range = 12-131)} \\
&\text{False positive} & = & 16 & 64\% \\
&\text{True positive} & = & 9 & 36\% \\
\end{align*}
\]

Histologically proven malignant cases with normal serum acid phosphatase levels = 43 82.69%
Raised acid phosphatase levels in Ca. prostate = 9 17.31%

Age:
The youngest patient was a 48 year old.
The oldest patient was a 93 year old.
Mean age = 70.84 years.

REVIEW OF ACID PHOSPHATASE

The significance of elevated acid phosphatase has been extensively
studied since the recognition by Gutman and Gutman\(^1\) in 1938 of its potential as a tumour marker. Numerous studies have revealed elevated serum concentrations in 65 to 85 percent of the patients with prostatic cancer metastases to bone and in as many as 34 percent without bony metastases\(^2\). The serum concentration of prostatic acid phosphatase in patients with prostatic cancer shows a paradoxical increase despite the known decrease in tissue concentration levels. This increase may be attributable to the increased mass of the prostate and the metastatic lesions if the mass is sufficiently large but notably more important are factors causing release of more of the enzyme into the circulation (ductal obstruction, invasion of lymphatics and blood vessels, and extension of the tumour beyond the prostatic capsule). It must be realized that serum acid phosphatase as measured by enzymatic assay or radioimmunoassay varies from hour to hour and day to day, with the amount of variation differing from patient to patient therefore the mean of several samples must be determined to obtain meaningful data\(^3\). Maatman et al found variations in prostatic acid phosphatase in radioimmunoassay of as much as 79\% above and 50\% below the mean during a 48-hour period in patients with stage D prostatic cancer\(^4\). Greatly elevated serum acid phosphatase has been documented by enzymatic and immunological methods in prostatic infarction with urinary retention. Concentrations decrease rapidly in the 24 hours after catheterization and return to normal after prostatectomy. Approximately 300\% of patients with prostatic infarction can have an elevated serum acid phosphatase concentration\(^5\). Cystoscopy and catheterization may elevate serum prostatic acid phosphatase transiently into the abnormal range, with normal values returning within 48 hours. The effects of digital examination and massage of prostate are more controversial. Most studies have shown no or only rare elevations by enzymatic assay or radioimmunoassay after simple rectal examination. Kendall found no elevation in patients without cancer but a 57 percent incidence after rectal examination in men with prostatic cancer\(^6\). However most investigators have found a significant incidence of abnormal elevations after massage, from 10 to 60\%. by enzymatic assay and radioimmunoassay\(^7\). Enzymatic and immunological assays require appropriate specimen handling if the results are to be valid. For example if the specimen remains at room temperature and the clot is not removed within several hours, the serum will show falsely elevated levels. Also in acidified serum the enzyme activity decreases within a day at temperatures above 22 \(\text{C}\)^8. From these reports it is evident that the samples be acidified with citrate and also placed on ice immediately after venipuncture. Serum acid phosphatase primary use lies in the staging and monitoring of the patients
with prostatic cancer, and not in the initial diagnosis of the disease. The failure to find an elevated serum acid phosphatase level in most patients with localized prostatic cancer probably reflects the lack of access of the tumour marker to the blood, before the primary cancer invades and metastasizes.

Discussion

The results of the study show that the majority of patients dealt with in our unit had benign prostatic hypertrophy and only 1 6.3%/ had carcinoma. The most frequent operative procedure performed was a transurethral resection with 86.79% of people undergoing it, along with an internal urethrotomy procedure. The latter being performed to decrease the incidence of post operative urethral stricture formation. In 92.16% of cases the serum acid phosphatase was equal to or less than 11 (Substrate used for testing was p- Nitrophenylphosphate). Raised serum acid phosphatase, was reported in 25 cases of which only 36% were true positive. The mean age of patients undergoing surgery in our unit was 70.84 (range 48-93) years.

It is evident from the above results and the review of literature that serum acid phosphatase is a helpful, albeit imperfect tumour marker. In recent years numerous studies have been carried out to compare the different biological markers. Prostate specific antigen has been consistently found to be better than acid phosphatase. Cancer antigen CA-50 and creatine kinase BB isoenzyme appear to be of little diagnostic value. In another series the serum samples from prostatic cancer patients showed elevated prostate specific antigen levels at diagnosis whereas 70% of these showed normal prostatic acid phosphatase values. In the follow-up, prostate specific antigen is a better marker than prostatic acid phosphatase to detect disease progression and seems to constitute an evolutive tumour mass index. Prostate specific antigen is the most sensitive, the earliest, and the most prognostically reliable marker for the diagnosis and follow-up of prostate cancer patients. In conclusion we would like to state that the serum acid phosphatase values obtained in our patients had prompted us to initiate this study. The results of which and discussions with the clinical biochemists have helped us in setting up a better protocol for sampling, specimen handling and biochemical evaluation of blood obtained from a patient presenting to the urology unit.
References


