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An Atypical Case of High Prostate Specific Antigen in a False-Positive Case of Benign Prostatic Hypertrophy/Hyperplasia: A Case Study

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Abstract

Background: Prostate-specific antigen (PSA) testing has long been used as a screening tool for prostate cancer. However, it is not without its limitations. In some cases, men may receive a false-positive PSA result, which can lead to unnecessary anxiety and concerns about their risk of developing cancer.

Aim: This study aims to reveal and discuss the case of a patient with a false-positive PSA value of 100 ng/mL.

Discussion/Conclusion: Depending on PSA assays as an all-seeing eye in detecting and screening for Prostate Cancers (PCa), may not be completely reliable. Studies have found its sensitivity and specificity questionable. Although current studies have put the borderline values between 4ng/mL and 10ng/mL, many studies have found PCa biopsy-positive cases at values lower than 4ng/mL and negative cases at values greater than 10ng/mL. Nevertheless, the concept of over-treating and overdiagnosis was also touched on.

Background

Prostate-specific antigen (PSA) is a protein produced by both normal and malignant cells in the prostate gland. The PSA test measures the level of PSA in the blood and has been the standard for prostate cancer screening for the past three decades. PSA testing, along with a digital rectal exam (DRE), is commonly used by healthcare providers to aid in detecting and monitoring prostate cancer. However, there is ongoing debate and research regarding the operating characteristics of PSA and its effectiveness in detecting prostate cancer.

PSA is a protein produced by the prostate gland and is normally present in small amounts in the blood. Elevated levels of PSA can indicate the presence of prostate cancer, but they can also be caused by other factors such as age, certain health conditions, and even sexual activity. The PSA test measures the level of PSA in the blood and is an important tool in the early detection of prostate cancer.

This study aims to reveal and discuss the case of a patient with a false-positive PSA value of 100 ng/mL.

Case History

A 78-year-old retired Muslim Civil servant presented to the Surgery Out-Patients Department (SOPD) on account of a two months history of lower urinary tract symptoms (LUTS), which were hesitancy, increased frequency, straining and occasional pain on urination. There were occasional moments of relieve, but symptoms were getting more frequent with shorter relieve intervals. In the past two weeks before presentation at our facility, intermittently he has had symptoms in keeping with Bladder outlet obstruction (BOO), with one previous episode necessitating urethral catheterization. There were no symptoms of haematuria, urethral discharge, sharp lower migratory inguinal pains or pyrexia. All other systemic reviews were relatively normal. He was a known hypertensive patient of 25 years who has been regular on his medications and follow-up, but he was not a known diabetic. He was placed on daily Duodart tablets, which contained o.4mg tamsulosin hydrochloride and o.5mg dutasteride, which gave some symptomatic relief.

On examination, he was an elderly man, who was not ill-looking. He was not pale, nor was he dehydrated, anicteric, afebrile (36.2°C) and nil pedal oedema. He was Oriented in Place, Time and Person. His mental state examination did not reveal any gaps or deficits. His pupils were 3mm bilaterally and equally reactive to light. His touch sensations on light and deep pricks were preserved and normal. He had normal tone and power on all limbs and had normal biceps, abdominal, cremasteric, patella and plantar reflexes. His abdomen was flat and moved with respiration. There was a grid-iron scar on the right iliac region. There were no areas of tenderness. There was also no renal angle tenderness when attempts to elicit them were made. The patient had a liver span of 10cm and the spleens were not palpable, nor kidneys ballotable. He had circumcised male genitalia, with no visible anomaly. No discharge at the external urethral orifice. Two testes were palpable in the scrotum and were not tender. He had satisfactory anal hygiene. No faeces were smearing the area around the anal canal. The anal sphincter properly gripped the examining finger. An enlarged prostate was palpated on Digital Rectal Examination (DRE), It was firm, smooth and non-tender. His radial arterial pulse was 84 beats per minute and his supine blood pressure (left arm) was 130/80mmhg.

His chemistry results showed Na (136mmol/l), K (5.0mmol/l), Urea (8.9mmol/l), Cr^- (162mmol/l), Cl^- (105mmol/l), CHO_3 (22mmol/l). Thus, showing an elevated creatinine level. PSA level was 100 ng/mL. The ultrasound scan showed an enlarged prostate (about 56 cc). Normal in outline and echotexture, with no masses, nor cysts identified. Baseline Haematological investigations conducted all came out within normal reference intervals for his age. Serology investigations for Human Immunodeficiency Virus and Hepatitis were non-reactive. Other parameters, such as uric acid, acid phosphatase and alkaline phosphatase were all within reference intervals.

Based on the high PSA levels, the patient was counselled for and consented to a Tru-cut prostate biopsy. Biopsy yielded no abnormal cell activity. However, the patient still consented to a complete prostatectomy. Subsequently, following the prostatectomy, the prostate sample was sent to the Histopathology lab, where multiple slices were prepared and stained. However, they assessed Benign Prostatic Hypertrophy/Hyperplasia. No signs of Malignancy were seen.

The patient has since been discharged, fully recovered and no longer has the LUTS. However, the impact of the seemingly unnecessary surgical procedures and medical treatment on his quality of life will remain personally known to him alone. Nevertheless, it remains debatable if we averted an eminent danger or merely acted based on a high index of suspicion and susceptible prevalence in the region.

Discussion

Although most health facilities operate with 4mg/mL as the upper limit for PSA assays, some exceptions are made for the elderly to about 5.5 ng/mL. Above this point, suspicions of Prostate Cancer (PCa) begin to arise, with or without LUTS. However, many studies conducted have questioned the specificity of PSA for the detection of prostate cancers. Some patients with PSA levels less than 4mg/mL have been found to have PCa while some with values greater than 10mg/ml have been found PCa-free [1]. Even in asymptomatic patients, the value of the PSA is considered the first day in a PCa possible diagnosis, even after a Tru-cut biopsy may have come up with nothing. This is because the tumour leading to high PSA levels can be missed, especially if it is very small, thus not completely exonerating the possibility of a PCa [2]. However, it is worth of note that not all PCa tumours will spread, cause symptomatic disturbances or ever be discovered. Such tumours are often discovered postmortem, with the person having died from other causes. This goes to show that not all PCa tumours need to be treated [3]. Nevertheless, the predictive indices of this decision are still not fully understood. Discovering such silent PCa tumours is often coincidental, and is known as Overdiagnosis and whereas, treating them is known as Overtreatment [3-4].

In patients with high PSA levels, the decision to keep treating is often made and supported by both the physician and the patient. Although, the autonomy fully resides with the patient. This is often influenced by knowledge of the fact that PCa is an aggressive type of cancer, is very prevalent in our setting, has a significant chance of being present with a high PSA, can be missed even on Tru-cut biopsy and also, the best chance of survival is found when treatment is commenced early. On the part of the patient, this may be fueled by anxiety and distress, especially in patients with high PSA levels, proportionally [2]. The worth note is the fact that a total transabdominal prostatectomy was done in this patient and completely analysed histologically, but found no tumours or dysplastic cells on microscopy. Hence, this qualifies as a false positive elevated PSA value. Some of the reasons that may cause a false positive PSA value associated with this patient were an increase in age, benign hyperplasia and Urinary tract Infections. Although, they may not fully explain the 100ng/mL assayed.

In a study that was carried out on the Prostate Cancer Prevention Trial (PCPT), the sensitivity of PSA and its thresholds (4ng/mL) were been called to question for detecting a little more than 20% of the PCa cases, whereas having more a specificity of more than 93% [5]. While this study may have praised the specificity of prostate cancer, our patient in this case study very well fell within the 6% that had false positive PSA elevated levels in the PCPT study. It is worth of note that further decreasing the globally accepted reference value for PSA screening in a bid to increase her sensitivity yield may only just lead to overtreating and overdiagnosis [5].

Notwithstanding, the atypical nature of the case described above begs the question of how specific an increase in PSA is for PCa. As values above 10ng/mL already raise malignant suspicions, whereas this patient had a PSA of 100 ng/mL and still had no cancer detected on biopsy and even complete slicing and preparation of his prostate post (total) prostatectomy. How specific then is PSA to PCa?

In 2018, a Harvard University Health Blog writer Charlie Schmidt wrote an article about how limited the abilities of PSA tests are as a tool to detect PCa was based on multiple internationally recognized studies conducted globally, he struck 3 main arguments;

1. PSA was not specific enough as such led to false positives among patients
2. There was no need for routine screening, as studies revealed that there were almost no distinguishable differences in the mortality rates between the screened and unscreened.
3. PSA screenings often led to overtreating and overdiagnosis. It was quoted that for every life saved, twenty-seven others got treatments for cancers that may have been harmless.

In the end, his article, like many others that he cited in his works caused doubts about PSA screening [6].

The Psychological Impact of False-Positive Results

Research has shown that men who receive a false-positive PSA test followed by a cancer-free biopsy may experience heightened worry about their subsequent risk of cancer. These individuals may also report more problems with sexual function compared to those with normal screening results. The psychological effects of false-positive results can be significant and may persist for several months [7].

Addressing the Limitations of PSA Testing

While PSA testing remains an important tool in early prostate cancer detection, it has its limitations. False-positive results can lead to unnecessary worry and potentially unnecessary medical procedures. To address these limitations, ongoing research should focus more on improving the accuracy of PSA testing and developing additional screening methods that can provide more precise information about an individual's risk of prostate cancer.

The Importance of Individualized Care

Each individual's situation is unique, and the decision to undergo PSA testing or pursue further diagnostic tests should be based on a thorough understanding of the risks and benefits. Healthcare providers need to consider the individual's preferences, medical history, and overall health when discussing prostate cancer screening options. Shared decision-making between the patient and the healthcare provider is key to ensuring that the best course of action is taken.

Conclusion

While the world still searches for other markers for the detection of PCa, we strongly rely on PSA assays. With 4ng/mL as the benchmark, more than 60% of positive cases are missed, whereas almost 10 per cent of false-positive cases are encountered too. For every true positive seen, about 1:27 cases are from otherwise harmless tumours that may never progress or metastasize. Such leads to overtreating and overdiagnosis.

False-positive PSA results can have a significant psychological impact on individuals, leading to increased worry and concerns about their risk of developing prostate cancer. It is important for healthcare providers to have open and honest discussions with their patients about the limitations of PSA testing and to address any concerns or anxieties. By providing clear information and individualized care, doctors can help alleviate unnecessary worry and ensure that patients have a realistic understanding of their risk. Continued research and advancements in screening methods are also necessary to improve the accuracy of prostate cancer detection and reduce the occurrence of false-positive results.

Abbreviations

PSA – Prostate Specific Antigen.
PCa – Prostate Cancer.
PCPT – Prostate Cancer Prevention Trial.
DRE – Digital Rectal Examination.

Conflict of Interest

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