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Case Report

Diagnosis of Prostate Cancer Recurrence with PSA Levels below 0.2 ng/ml with Intermittent Antiandrogen Therapy

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Abstract

A case of investigation of a patient with recurrent prostate cancer after Radical Prostatectomy (RP) followed with 70 Gray irradiation (RT) due to numerous positive margins is reported . The Prostate Specific Antigen (PSA) level was fluctuating below 0.2 ng/mL . Comprehensive data on symptoms, Ultrasound (US) measurements, medical treatment, and PSA level fluctuations during intermittent Antiandrogen Therapy (ADT) were analyzed. ADT led to reduction in the size of the cancer by almost half. The PSA level decreased in accordance with the ADT injections. US with Doppler showed an area with increased blood flow. A nano-knife procedure was applied to this suspicious area. Then the Pfizer vaccine was administered , as a result of the final two treatments the PSA level dropped to 0,006 ng/ml. All the symptoms disappeared.

Introduction

Prostate cancer is the most common cause of death among men. The earlier the cancer is detected, the greater the chance of a complete cure. Today, there are several classic diagnostic methods: PSA level, US, X-ray (CT) and Magnetic Resonance Tomography (MRI), biopsy. The most difficult situation is when a patient has prostatitis with symptoms similar to cancer that masks oncology. After RP, the PSA level of 0.2 ng/ml is the standard for recognizing cancer recurrence and initiating medical treatment. An elevated PSA level, but below 0.2 ng/ml, does not qualify as cancer, and the recommendation to wait until the PSA level rises 0.2 ng/ml is standard. However, in this case there is a risk of cancer cells spreading and metastasizing, and additional tests to detect possible cancer will reduce the likelihood of a bad situation in the future. The probability of recurrence can be as high as 40%, depending on the treatment used and the properties of the cancer. Early detection of prostate cancer recurrence after RP or/and RT is very important. PSMA-Ga and other methods give about a 50% chance of detecting cancer with a low PSA level. This article presents the case of investigation and treatment of one patient with recurrent prostate cancer with a low PSA level.

The aim of the article is to analyze what has been done and what can be done better, due to the huge number of patients with similar recurrence with low PSA levels.

Results

The patient has been suffering from prostatitis since 2003. Classic symptoms with frequent urination, but no pain in pelvic. PSA level was below 4 ng/ml for many years. Lower back pain was almost constant, but was associated with a protrusion about 5 mm long in the spine. In June 2016 urination became very frequent, so PSA level was measured and was 9 ng/ml. The PSA in Kyiv was measured with electrochemoluminescent analysis, Roche Diagnostics, Analyzer: Cobas 8000/Cobas Pro/ Cobas 6000/Cobas (Switzerland). The patient was 59 years old (in 2016). A biopsy was scheduled as late as in November 2017. PSA at that time was 14 ng/ml. This indicates the cancer had

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grown by 1.5 times while the patient was waiting for the biopsy. After the biopsy all the ten needles had cancer, some of them up to 90%. The most aggressive type of cancer with a Gleason score of 9 was found in one needle, while the rest had Gleason scores between 6 to 8. Before the surgery, Neither ADT nor a 3D model of the tumor was made. The surgery was performed on January 9, 2017 with a Da Vinci robot. Four lymph nodes were cut out from left side, and eight from the right. Pathological examination showed multiple positive margins throughout the excision area. The largest piece of left tumor measured 4 mm . The T3 M0 N0 R1 prostate cancer was approximately 6 cm in size. A piece of prostate and seminal vesicles remained in the pelvis. There was severe lymphadenopathy after surgery (12 x 51 mm right, 37 x 82 mm left). The drainage was installed for two weeks.

Immediately after surgery the PSA level was 0.68 ng/ml, which confirmed a large number of positive margins. ADT was recommended to stop the cancer growth several months before RT, reduce cancer volume, and increase the likelihood of cancer elimination during RT [1-3]. 10.3 mg of diphereline was injected in March 2017. A month later, the PSA level decreased to 0.4 ng/ml, indicating the success of the ADT. The PSA level dynamics is presented in Figure 1. RT was started in May 2017. Over a period of two months, 39 sessions of 1.8 gray doses were applied. Another dose of 10.3 mg of diphereline was injected in June 2017.

After RT in combination with ADT, the PSA level was 0.004 ng/ml (end of August 2017). But in December 2017, the PSA level was 0.092 ng/ml. This PSA level indicated a high risk of having live cancer cells [4-7]. The patient felt a mild inflammation in the pelvic. Soon the symptoms of inflammation disappeared. The PSA level decreased to 0.058 ng/ml. Three years later, inflammation in the pelvic reappeared, but in a severe form. An US showed that a small lump in the pelvis on the inguinal surface between the urethra and rectum had increased in size (Figure 2 comparing a and b). The PSA level increased to 0.167 ng/mL, suggesting the presence of viable cancer cells.

No treatment was performed, and after 6 months, the PSA level decreased to 0.04 ng/ml. This may be due to the immune system, activated by the products of cancer cell death after RT, recognized and killed active cancer cells. Six months later, PSA level increased to 0.07 ng/ml, and severe lower back pain was managed with four dexamethasone injections administered into the lumbar spine to relieve the pain.

In January 2022 an US showed an 8 x 18 mm sized bubble in the pelvic. There were no symptoms during this period. In August 2022, a US scan showed , that this bubble had almost doubled in size to 18 x 28 mm size toward the bladder and adhered to the bladder (Figure 1 inset, Figure 2, red arrow). The "finger" from this knob touching the bladder is visible on the US image. The blue arrow indicates another suspicious region, later identified as an unremoved seminal vesicle that had shifted position. The Pfizer vaccine was administered in September 2022, *(Disclaimer-While this temporal association is notable, a direct causal relationship between vaccine administration and PSA reduction cannot be confirmed.)* Two weeks later, pelvic pain and inflammatory symptoms developed . A CT showed a flesh lump on the surface of the perineum, which confirmed the data of the US. According to the CT doctor, it was a piece of prostate left behind during surgery. It is known that aggressive cancer with Gleason 9 can occur even with a low PSA level. The recommendations of professor oncologist in Germany were chilling: it is difficult to do a biopsy, it is difficult to treat a possible relapse, treatment will be considered only when the PSA level rises to the value of the German protocol. The patient"s opinion: if left untreated, the cancer will grow into

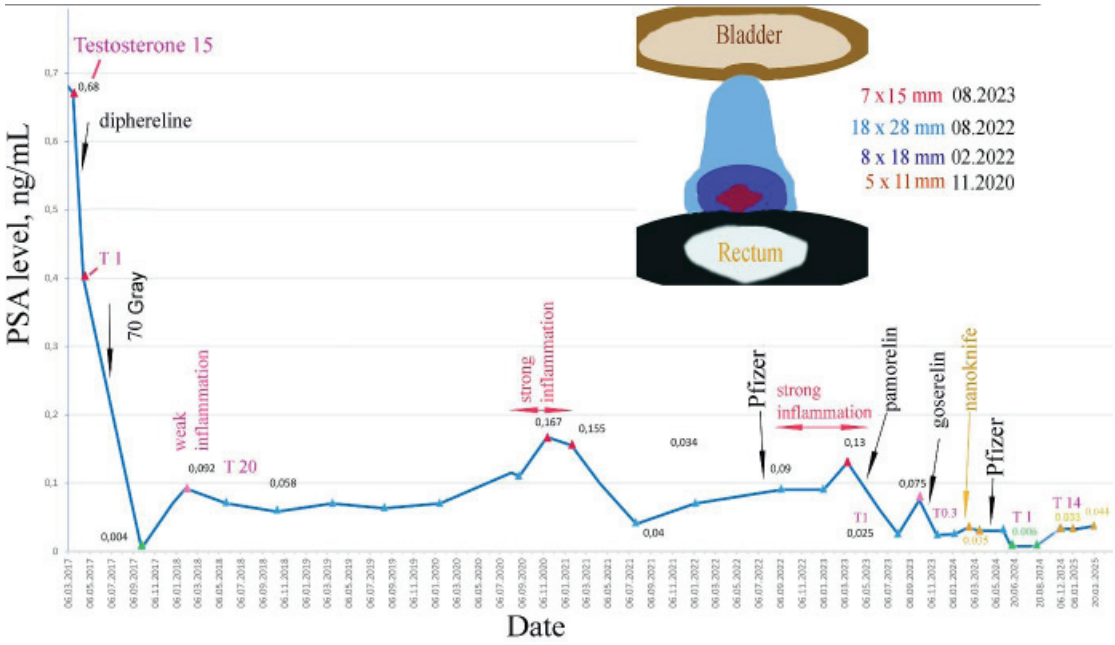

Figure 1: Evolution of PSA level in correlation with symptoms and treatment. The inset shows a scheme of the evolution of the tumor topology.

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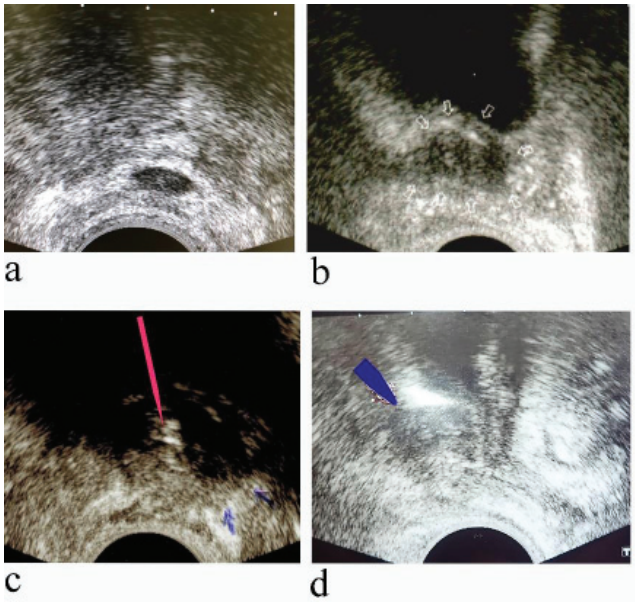

Figure 2: Evolution of the cancer topology by US: a. 11.2020, b. 09.2021, c. 08.2022. d. 04.24.

the bladder wall. Since the patient underwent RT, surgery will not be possible, only death is predicted if the tumor does not undergo treatment before it grows into the bladder. A German professor recommended that the patient, who had Techniker Krankenkasse insurance, seek a consultation in Kyiv.

There was constant pain and urination every hour, even at night. An MRI was performed in Germany in February 2023 . It should be emphasized, that numerous MRI scans made both in Kyiv and in Germany did not reveal cancer. The PSA level measured at that time was 0,13 ng/ml. After these test results, another German oncologist decided to inject 3,75 mg of pamorelin. She informed the patient that if the PSA level is below 0.2 ng/ml, the advanced tests such as PSMA-Ga are not covered by insurance, and the patient would have to pay in full, if patient believes advanced tests are necessary. The result was a 5-fold decrease in PSA level: to 0,025 ng/ml in a month (Figure 1). This indicated the presence of live castrate-sensitive cancer cells. An MRI scan in August 2023 revealed the tumor had reduced in size by half , and the "finger" that had grown in 2022 and touched the bladder had shortened and no longer touched the bladder. Thus, the risk of cancer invading the bladder wall has disappeared. However, the PSA level after the end of the ADT quickly tripled to 0.075 ng/ml, which, despite tumor shrinkage, still indicated the presence of cancer compared to the PSA level of 0.025 ng/ml during the ADT. Doppler ultrasound revealed increased blood flow within and surrounding the node. In December 2023, an injection of goserelin with dose of 10.25 mg was performed, which led to decrease in PSA level to 0.025 ng/ml. The patient"s opinion was that these results and symptoms pointed out to the presence of tumor. Numerous US and MRI investigations were made, and the results were shown to many doctors in Kyiv. Two US doctors and two professors recognized the results as the evidence of a small tumor. The treatment of the tumor was recommended. The option of radio-frequency burning was considered, but the tumor was located between the bladder wall and the rectal wall, so it was not recommended because of possible damage to these walls.

The nano-knife procedure (irreversible electroporation) was performed on February 9, 2024 . Only the central part of the suspicious area, namely shrunk knob, was treated. The rise in PSA from 0.025 ng/mL to 0.035 ng/mL suggested cancer cell destruction . An MRI performed shortly after the procedure showed that the tumor had been necrotized. In April 2024, the PSA level was 0.03 ng/mL . This can be explained by production of PSA by semen bubbles remaining in the pelvis and/or the presence of live cancer cells. The Pfizer vaccine was administered in April 2024. Symptoms of inflammation and bladder pain disappeared. The PSA level dropped to 0.006 ng/ml, which indicates a high probability of complete cancer cells death. Since that time, there have been no symptoms that were present with cancer: no frequent urination, no pelvic inflammation, no pain in lower back, no pelvic sensitivity to cold, no increased libido. While the PSA drop followed Pfizer vaccine administration, this observation remains anecdotal. Further clinical studies are needed to evaluate any potential immunological role. It should be mentioned that two injections of the Moderna vaccine given before Pfizer showed no reaction from the tumor. Testosterone and PSA levels remained low through October 2024. It was the cumulative effect of the nano-knife, ADT and Pfizer that led to the PSA level dropping to 0,006 ng/ml in three months. It should be noted, that the PSA level, under the influence of ADT for one month (prior to the nano-knife procedure), was 0.03 ng/mL. This can be due to presence of some castrate-resistant cancer cells. It is possible that the nano-knife ablated residual castrate-resistant cancer cells in the shrunken knob. The PSA level increased to 0.044 ng/mL after testosterone levels rose to 14 ng/mL is highly likely to indicate of living cancer cells. Determining whether they are located in the pelvic or elsewhere remains challenging with current diagnostic techniques.

Conclusion

1. For large localized prostate cancer, ADT should be used before surgery. This reduces the size of the tumor to be excised, increasing the rate of success.
2. Intermittent ADT and monitoring the fluctuation (if) of PSA level is a cost-effective and practical method of diagnosis of prostate cancer recurrence when PSA level is below 0,2 ng/ml.
3. To make a correct diagnosis, it is necessary to analyze a set of symptoms, analyzes and measurements.
4. The nano-knife is a good method for treating localized recurrence when other, more energetic methods are dangerous to damage neighboring tissues.
5. Activation of the immune system can help to kill cancer.

Ethical Considerations

The patient provided informed written consent for the publication of this case report and the use of clinical data and imaging.

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