

## Over 5 Years of Complete Antiandrogen Withdrawal Response in a Patient with Prostate Cancer: A Case Report

Ryoo H<sup>#</sup>, Choi J<sup>#</sup>, Ryu JH, Kim YB, Yang SO, Lee JK and Jung TY\*

Department of Urology, VHS Medical Center, Seoul, Korea

<sup>#</sup>Both authors contributed equally as a primary author

### \*Corresponding author:

Tae Young Jung,  
Department of Urology, VHS Medical Center,  
53 jinhwangdo-ro 61-gil, Gangdong-gu, Seoul  
05368, South Korea, Tel; 82-2-2225-1739,  
Fax; 82-2-2225-1844,  
E-mail; urodoct@bohun.or.kr

Received: 15 Sep 2021

Accepted: 25 Sep 2021

Published: 30 Sep 2021

### Copyright:

©2021 Jung TY. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and build upon your work non-commercially.

### Citation:

Jung TY, Over 5 Years of Complete Antiandrogen Withdrawal Response in a Patient with Prostate Cancer: A Case Report. *Ann Clin Med Case Rep.* 2021; V7(10): 1-4

### Keywords:

Prostate cancer; Antiandrogens; Prostate-specific antigen

### 1. Abstract

Progressive prostate cancer is primarily treated with androgen-deprivation therapy. The antiandrogen withdrawal (AAW) response (AAWR) is defined as subjective and/or objective improvement following antiandrogen cessation in patients with elevated prostate-specific antigen (PSA) levels treated with combined androgen blockade (CAB). Regarding the duration of AAWR, only a few cases showing long-term complete responses based on PSA decline have been reported. We report the case of a patient who received CAB and survived for >60 months since AAW despite the metastatic disease. A 64-year-old male patient visited our outpatient clinic in July 2011 with weak stream and tingling sensation of bilateral legs. He had an initial PSA of 185 ng/ml and was diagnosed with prostate cancer T3bN0M1b. CAB was administered in August 2011, with a regimen of 3.75 mg of triptorelin acetate and 50 mg of bicalutamide. The PSA reached a nadir at 0.007 in December 2012; however, this increased to 16.39 in July 2016, 5 years after initiation of treatment. The author decided to discontinue bicalutamide to achieve AAW, which resulted in the dramatic decrease of the patient's PSA to 5.33, 2.16, and 0.491 for 3 consecutive months. The PSA reached nadir again in August 2017, 1 year after bicalutamide discontinuation. No other medications were administered to the patient to treat prostate cancer, which was well-maintained with PSA < 0.003 until June 2021. Although the prolonged survival time seen in our present case is rare, AAW is a potential treatment option for patients with advanced prostate

cancer even with metastatic disease.

### 2. Introduction

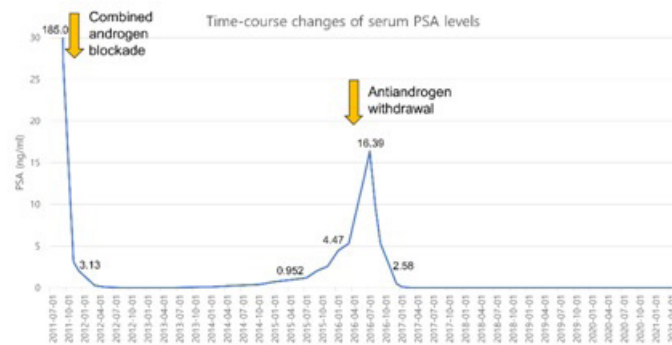
Progressive prostate cancer is primarily treated with androgen-deprivation therapy. Using an oral antiandrogen, such as bicalutamide, with or without androgen receptor blockade, is the main treatment for metastatic hormone-sensitive prostate cancer. It occasionally causes an antiandrogen withdrawal response (AAWR), which is generally defined as subjective and/or objective improvement following the cessation of an antiandrogen in patients with elevated prostate-specific antigen (PSA) levels, who are treated with combined androgen blockade (CAB) [1]. Regarding the duration of AAWR, only a few cases showing complete responses based on PSA decline have been reported. Here, we report the case of a patient who received CAB, with a long duration of complete response.

### 3. Case Report

A 64-year-old male patient visited our outpatient clinic in July 2011 with weak a stream and a tingling sensation on bilateral legs. His initial PSA was 185 ng/ml. The 8-core systematic biopsy was implemented, adenocarcinoma was identified on all cores, and the Gleason score was 8(4 + 4). The patient was suspected of pulmonary, liver, sacrum, and rib metastasis after image workup; hence, the patient was diagnosed with prostate cancer T3bN0M1b. CAB was administered in August 2011, with a regimen of 3.75 mg of triptorelin acetate and 50 mg of bicalutamide. The kinetics

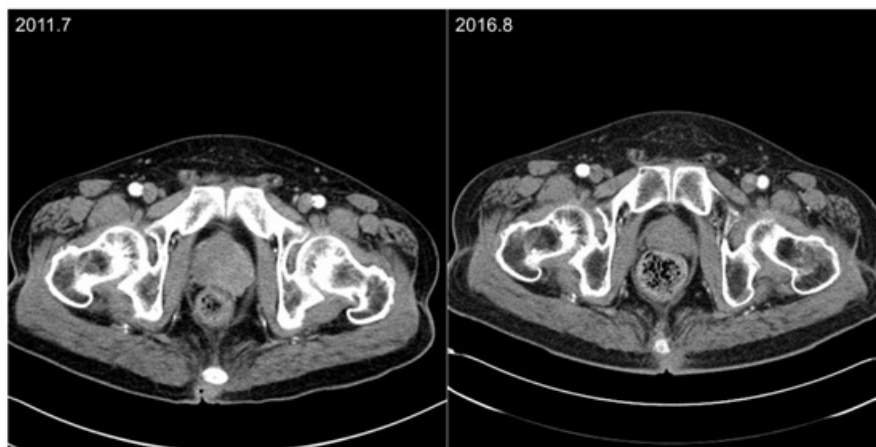
of PSA during treatment is displayed in Figure 1. The serum level of PSA decreased to  $<0.003$  ng/ml, and the patient's symptoms also improved. The PSA reached a nadir at 0.007 in December 2012; however, it increased to 0.204 in April 2014 and gradually increased further to 2.03 in September 2015. CAB was continued, and the PSA reached 16.39 in July 2016. In August 2016, an imaging workup was implemented, which revealed that the prostate remained shrunken and the nodule in the lungs had fibrosed. No lesions were observed in the liver, and there was no other suspected metastasis, including lymph nodes (Figure 2). The bone scan also showed no previous sacrum and rib lesions aside from lesions on

the left leg due to previous trauma (Figure 3). The author decided to discontinue bicalutamide to achieve an antiandrogen response. The patient's PSA decreased dramatically to 5.33, 2.16, and 0.491 for 3 consecutive months, reaching nadir again in August 2017. No other medications were administered to treat the prostate cancer, which remained well-maintained with a PSA  $< 0.003$  until June 2021. About 9 years and 10 months after the initial CAB, the total testosterone remained at castration level and was 0.471 ng/ml in June 2021. In the present study, written informed consent was obtained from the patient to publish the present case report and any accompanying images.



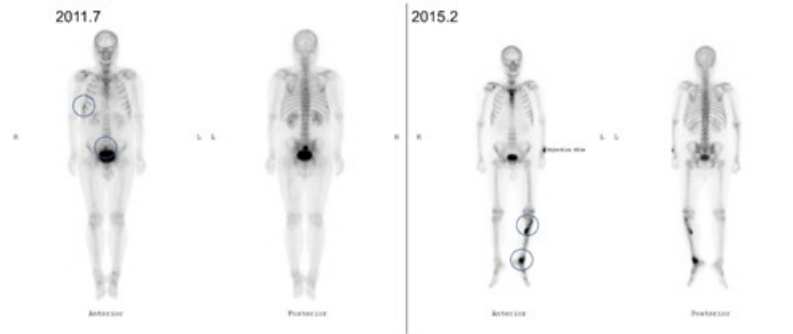
**Figure 1: The kinetics of prostate-specific antigen during treatment**

Prostate-specific antigen changes and applied treatments for patients in the 10 years. During that period, the testosterone was maintained at the castration level.



**Figure 2: Computed tomography findings during treatment.**

Initial computed tomography indicated a 3.5-cm well-enhancing mass with focal outward bulging into the adjacent perirectal fat in the left prostate, suspected to be prostate cancer. In the follow-up image, the prostate-specific antigen increased to 16.39; however, the prostate shrank and was not enhanced in the arterial phase.



**Figure 3: Bone scan findings during treatment.**

The initial bone scan image revealed suspected metastasis to the right rib and sacrum; however, the lesion receded after combined androgen blockage treatment. Only trauma-induced lesions were observed in the left leg.

#### 4. Discussion

The AAWR was first reported by Kelly and Scher in 1993 [2], who observed a PSA decrease (36%–89% decline) following discontinuation of the non-steroidal antiandrogen, flutamide. Additionally, AAWR has been reported following the discontinuation of bicalutamide [3]. Suzuki et al. reported that the PSA decrease (15.5% decline) was observed following the discontinuation of bicalutamide and that the mean response duration was  $5.8 \pm 3.8$  months [4]. Sator et al. suggested that the duration of antiandrogen use prior to withdrawal is a predictor of AAWR [5]. They reported that only the duration of prior antiandrogen use was a significant predictor of PSA decrease after AAW. According to their report, patients who received antiandrogen for a longer duration prior to withdrawal showed AAWR more than patients treated with antiandrogen for a shorter duration. Additionally, Sher et al. reported an association between the duration of antiandrogen use prior to withdrawal and the frequency of AAWR [6]. In their study, patients with a PSA decrease greater than 50% from the baseline were treated with a longer duration of antiandrogen compared to patients with a PSA decrease of less than 50% from the baseline (25 months vs. 16 months,  $p = 0.012$ ). However, not all studies showed an association between the duration of antiandrogen use prior to withdrawal and AAWR. Herrade et al. reported that there was no significant association between the duration of AA use and AAWR [7]. In their study, there was no significant difference in the median months of antiandrogen use prior to withdrawal between AAW responders and AAW non-responders (19 months vs. 16.5 months,  $p = 0.41$ ). In our present case, contrary to Herrade's study, it seems that the duration of antiandrogen use is associated with AAWR. The patient received bicalutamide for 5 years prior to withdrawal. Some studies reported about survival following AAW, such as that by Sator et al. stating that the median overall survival following AAW was 22 months [5]. Small et al. reported a nonsignificant

increase in total survival time after starting hormonal therapy for responders to AAW of 44.5 months compared with 35 months for non-responders [8]. In terms of the median survival time after initiation of the AAW, they reported that it was 13 months for responders and 12 months for non-responders. However, in our present case, the patient has survived for >60 months since AAW despite the metastatic disease. Mean survival time in patients with hormone-resistant prostate cancer is relatively short. Therefore, prolonged survival, even if it will only be a few months, would be a significant gain for these patients with advanced disease. Thus, AAW could be a good treatment option for patients with advanced prostate cancer, and it could contribute to the prolongation of survival.

#### 5. Conclusions

Although the prolonged survival time seen in our present case is rare, the AAW should be considered a potential treatment option for patients with advanced prostate cancer even with metastatic disease.

#### 6. Funding

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2021R1F1A1048198) and by VHS Medical Center Research Grant, Republic of Korea (VHSMC21039) to T. Jung and J. Choi.

#### References

1. Paul R, Breul J. Antiandrogen withdrawal syndrome associated with prostate cancer therapies: incidence and clinical significance. *Drug Safety*. 2000; 23(5): 381-390.
2. Kelly WK, Scher HI. Prostate specific antigen decline after antiandrogen withdrawal: the flutamide withdrawal syndrome. *J Urol*. 1993; 149(3): 607-609.
3. Small EJ, Carroll PR. Prostate-specific antigen decline after casodex

withdrawal: evidence for an antiandrogen withdrawal syndrome. *Urolog*. 1994; 43(3): 408-410.

4. Suzuki H, Okihara K, Miyake H, Fujisawa M, Miyoshi S, Matsumoto T, et al. Alternative nonsteroidal antiandrogen therapy for advanced prostate cancer that relapsed after initial maximum androgen blockade. *J Urol*. 2008; 180(3): 921-927.
5. Sartor AO, Tangen CM, Hussain MH, Eisenberger MA, Parab M, Fontana JA, et al. Antiandrogen withdrawal in castrate-refractory prostate cancer: a Southwest Oncology Group trial (SWOG 9426). *Cancer*. 2008; 112(11): 2393-2400.
6. Scher H, Zhang Z, Cohen L, Kelly W. Hormonally relapsed prostatic cancer: lessons from the flutamide withdrawal syndrome. *Advances in urology*. 1995; 8: 61-95.
7. Herrada J, Dieringer P, Logothetis CJ. Characterization of patients with androgen-independent prostatic carcinoma whose serum prostate specific antigen decreased following flutamide withdrawal. *J Urol*. 1996; 155(2): 620-623.
8. Small EJ, Srinivas S. The antiandrogen withdrawal syndrome. Experience in a large cohort of unselected patients with advanced prostate cancer. *Cancer*. 1995; 76(8): 1428-1434.