Oncology

Complete Response to Bicalutamide Withdrawal Prolonged for Almost 2 Years in Patients With Metastatic Prostate Cancer

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A R T I C L E   I N F O

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A B S T R A C T

This is the first case report describing a complete response to bicalutamide withdrawal that lasted for almost 2 years in a patient with metastatic prostate cancer. An 80-year-old man who had prostate-specific antigen (PSA) level elevation (168.1 ng/mL) visited our hospital in February 2010. Bone scintigraphy showed pelvic metastases. We started hormonal therapy with leuprorelin and bicalutamide. The PSA concentration decreased to <0.1 ng/mL but started increasing again and reached 1.64 ng/mL in October 2012, at which time bicalutamide administration was discontinued. The PSA concentration decreased again and has remained below the limit of sensitivity for almost 2 years.

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Introduction

Cancer of the prostate is the most prevalent cancer in American men. Metastatic prostate cancer is primarily treated by testicular androgen ablation (medical or surgical). Nonsteroidal antiandrogens are commonly used with luteinizing hormone-releasing hormone analogs for metastatic prostate cancer.

Withdrawal responses after estrogenic therapy for breast cancer were reported in 1986. Withdrawal responses in prostate cancer patients were initially documented after treatment with flutamide. Since then, withdrawal responses after other antiandrogens have been reported in prostate cancer cases.

Some cases respond well to antiandrogen withdrawal, with a >50% decline in prostate-specific antigen (PSA) level, but the duration of remission is limited to approximately 6 months.

We report here a patient with metastatic prostate cancer who had complete remission for almost 2 years after bicalutamide withdrawal.

Case presentation

An 80-year-old man visited our hospital in February 2006 for further evaluation of PSA level elevation, which was 168.1 ng/mL. A stony hard nodule was found in the right lobe of the prostate on digital rectal examination. The patient had hip pain. We strongly suspected metastatic prostate cancer. We scheduled a prostate biopsy within a few weeks, but he experienced an acute myocardial infarction and was admitted to the cardiovascular department of our hospital before the biopsy. Magnetic resonance imaging performed during hospitalization showed a gadolinium-enhanced tumor with a low T2 signal in the right lobe of the prostate. Bone scintigraphy showed metastatic tumors in the hip bone and pubis (Fig. 1). We made a diagnosis of poorly differentiated prostate cancer based on a physical examination and imaging test without the prostate biopsy because of the limitations of the indication. Hormonal therapy with leuprorelin and bicalutamide was started. The PSA concentration decreased to <0.1 ng/mL in 3 months, but started increasing again from the beginning of 2010, and reached 1.64 ng/mL in October 2012. The hip pain worsened and the alkaline phosphatase level rose to 453 IU/L. Bicalutamide administration was discontinued. The PSA concentration started declining again after a month, and dropped to <0.01 ng/mL within 3 months. The pain was resolved and the alkaline phosphatase concentration decreased to a normal level. The concentration of testosterone remained under 0.1 ng/mL after bicalutamide withdrawal. The PSA concentration has remained below the limit of sensitivity till date, which is almost 2 years (Fig. 2).

Discussion

Antiandrogen withdrawal syndrome with flutamide was first reported in 1993. Since then, withdrawal responses after other antiandrogens have been reported in prostate cancer cases.

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Discontinuation of antiandrogens can decrease the PSA level and reduce symptoms related to prostate cancer. There are thought to be many different mechanisms involved in the antiandrogen withdrawal syndrome. These include mutation of the androgen receptor gene and its coregulatory proteins and activation of the signal transduction pathways that may not involve the androgen receptor pathway. It is also possible that no single mechanism is utilized in each case.

The response rate of antiandrogen withdrawal, which is defined as more than a 50% decline in the PSA level, is about 30%. A declining PSA level is seen within 4-8 weeks after discontinuation of antiandrogens. The duration of the response to antiandrogen withdrawal is limited to approximately 3-6 months. It was reported in 2008 that a lower (<10 ng/mL) baseline PSA level, no metastasis, and longer duration of antiandrogen use were predictors of prolonged antiandrogen withdrawal. There have been reports of a sustained decline in PSA level <1 ng/mL for 1-2 years after antiandrogen withdrawal. However, there have been no reports of complete remission of PSA level, that is, <0.01 ng/mL, for several years after bicalutamide withdrawal. In the present case, we found the PSA level had remained below the limit of sensitivity for almost 2 years after bicalutamide withdrawal. We believe this to be a very rare case.

It remains uncertain whether responders of androgen withdrawal have a better prognosis. Antiandrogen withdrawal syndrome is not included in therapeutic options for castration-resistant prostate cancer in the 2014 European Association of Urology guidelines. However, in Japan the only therapy currently available for metastatic castration-resistant prostate cancer is docetaxel-prednisolone therapy, which often has strong adverse effects. Our patient has maintained an excellent physical condition for almost 2 years without such side effects. Bicalutamide withdrawal clearly contributed to an improvement of the quality of life of this patient.

Conclusion

We have described a patient whose PSA level remained below the limit of sensitivity for almost 2 years after bicalutamide withdrawal. Further study of the antiandrogen withdrawal response rate and the duration of PSA decline for each drug withdrawal is needed, which may contribute information concerning the choice of first-line antiandrogen drugs.

Consent

Informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflicts of interests

The authors declare that they have no conflict of interests.

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