JOURNAL OF
CONTEMPORARY MEDICINE

DOI: 10.16899/jcm.1175879
J Contemp Med 2022;12(6):1033–1035

Case Report / Olgu sunumu

Prolonged Response with Enzalutamide in a Prostate Cancer Patient on Hemodialysis

Hemodiyalize Giren Prostat Kanserli Hastada Enzalutamid ile Uzun Yanıt

Özge Kama Başcı[1], Ferhat Ekinci[2], Gonca Akdere Ateş[3], Atike Pınar Erdoğan[3], Ahmet Dirican[4]

[1]Balıkesir State Hospital, Department of Internal Medicine, Balıkesir, Turkey
[2]Şırnak State Hospital, Department of Medical Oncology, Şırnak, Turkey
[3]Manisa Celal Bayar University School of Medicine, Department of Medical Oncology, Manisa, Turkey
[4]İzmir Economy University School of Medicine, Department of Medical Oncology, İzmir, Turkey

Abstract

Current therapies in oncology that offer a longer and better quality of life are leading to more cases where cancer and chronic diseases coexist. Enzalutamide is a second-generation anti-androgen agent, was approved by the US Food and Drug Administration (FDA) in 2012 for the treatment of metastatic castration-resistant prostate cancer (mCRPC). There is no series with a large number of patients on the use of enzalutamide in patients with end-stage renal disease (ESRD). We present a patient diagnosed with mCRPC who was followed up with enzalutamide treatment for about 5 years after progression with docetaxel and who was on hemodialysis 3 days a week.

Keywords: Enzalutamide, prostate cancer, renal failure

Öz

Onkolojide daha uzun ve kaliteli bir yaşam sunan güncel tedaviler, kanser ve kronik hastalıkların bir arada görüldüğü vakaların artmasına neden olmaktadır. İkinci nesil bir anti-androjen ajan olan enzalutamid, metastatik kastrasyona dirençli prostat kanseri (mCRPC) tedavisi için 2012 yılında ABD Gıda ve İlaç Dairesi (FDA) tarafından onaylanmıştır. Son dönem böbrek hastalığı (SDBH) olan hastalarda enzalutamid kullanımına ilişkin çok sayıda hasta içeren bir seri bulunmamaktadır. Bu çalışmada, dosetaksel ile progresyon sonrası yaklaşık 5 yıldır enzalutamid tedavisi ile takip edilen ve haftada 3 gün hemodiyalize giren mCRPC tanılı bir hastayı sunuyoruz.

Anahtar Kelimeler: Enzalutamid, prostat kanseri, böbrek yetmezliği

INTRODUCTION

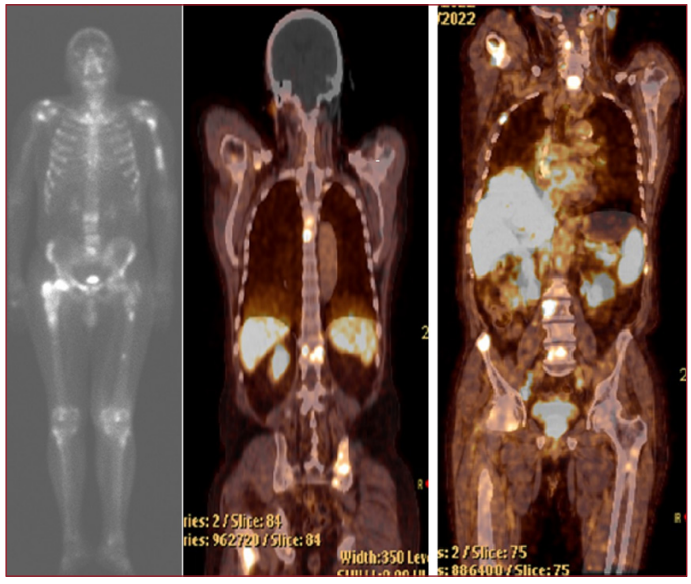
Castration-resistant prostate cancer (CRPC) is defined as a progressive disease that can be detected by elevated serum total prostate-specific antigen (PSA) levels or imaging methods, although the serum testosterone level is at the castration level (<50 ng/ml) (1). Enzalutamide, an androgen receptor signaling inhibitor, is one of the first-line therapies for (mCRPC). There are no adequate studies of recommendations or dose reduction for patients with renal impairment or ESRD. In this study, we presented a patient with a diagnosis of mCRPC who underwent hemodialysis (HD) and received enzalutamide for more than 5 years.

CASE REPORT

A 79-year-old male was diagnosed with prostate adenocarcinoma with bone metastases in 2011, with a Gleason score of 5 + 4, and treated with goserelin, bicalutamide and zoledronic acid by urology clinic. There was a history of bilateral grade 2 hydronephrosis and post-renal acute kidney injury to chronic kidney disease. He applied with the low back pain and PSA elevation in 2016. Laboratory findings were: PSA 19 ng/mL, creatinine 2,41 mg/dL, glomerular filtration rate (GFR) 25,6. Extensive bone metastasis with Technetium 99m-methyl diphosphonate (99mTc MDP) involvement was observed in bone scintigraphy (**Picture 1**). Abdomen magnetic resonance

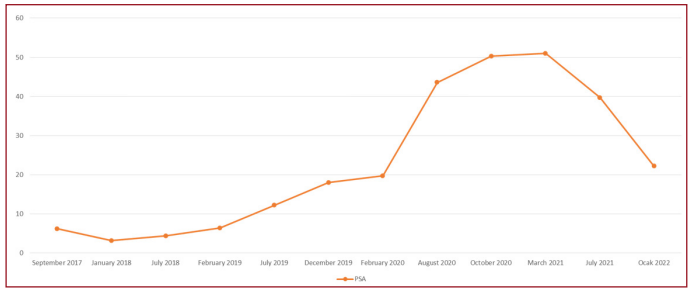
Corresponding *(İletişim)*: Özge Kama Başcı, Balıkesir State Hospital, Department of Internal Medicine, Balıkesir, Turkey
E-mail *(E-posta)*: ozgee.kama@gmail.com
Received *(Geliş Tarihi)*: 15.09.2022 **Accepted *(Kabul Tarihi)*:** 19.09.2022

imaging (MRI) showed enlarged pelvic and aortocaval lymph node metastases, 2 cm prostate lesion in the right posterior and the central zone. Docetaxel (75 mg/m^2) was planned for the patient with GFR 16. PSA levels elevated to 28,2 ng/ml after 2 cycles and decreased to 19 ng/ml. At the end of 6 cycles, the lesions were stable on bone scintigraphy, while abdominal MRI showed almost complete disappearance of lymph nodes and the lesion in the periprostatic area, regression to 13 mm of the lesion in the central zone.



Picture 1. Ga-68 PSMA PET/CT scan images of the patient over the years

Creatinine progression, anuria, metabolic acidosis developed before the 16th cycle (July 2017), he was taken to the routine HD program continued 2 days a week. Serum PSA elevated to 6.2 ng/ml and progression was observed in bone scintigraphy in September 2017. Enzalutamide (160 mg/day) was started as a step treatment. PSA level decreased to 3.9 ng/ml in a month, clinic-radiologically findings were stable for 2 years (**Graphic 1**).



Graphic 1. Prediction of PSA with enzalutamide treatment

Gallium-68 prostate-specific membrane antigen positron emission tomography (Ga-68 PSMA PET) taken in September 2019; progression was observed with diffuse metastatic lesions in the skeletal system and diffuse metastatic lymph nodes in the pelvis, PSA level was 12.2 ng/ml (**Picture 1**). Enzalutamide was continued because the patient was asymptomatic. Next scan showed stable lesions in prostate gland and pelvis, progression in skeletal diffuse metastatic lesions in September 2020, PSA was elevated from 19,7 ng/ml to 42,6 ng/ml in six months. There was a simultaneous increase in parathormone (PTH) levels (449 pg/ml) of the patient who were missed the nephrology follow-ups. HD sessions were increased to 3 days per week. The PSA level first decreased and then stabilized with a fluctuating pattern (**Graphic 1**). One year later, PSA was 44,8 ng/ml and PET scan findings were stable. Radiotherapy (RT) was applied to shoulders and right leg because of severe pain in July-September 2021. PSA levels decreased to 30,1 ng/ml and stayed similar levels during for 9 months.

Ga-68 PSMA PET/CT taken in February 2022 compared with in October 2021; PSMA expression in the prostate gland was stable, metastatic lymph nodes were stable, and metastatic lesions detected in both humeri, left iliac bone and femurs were regressed, other areas of the skeletal system were stable (**Picture 1**).

The patient is currently continuing on hemodialysis 3 days a week and has been on enzalutamide therapy for 58 months.

DISCUSSION

Advances in cancer treatments and dialysis techniques have increased the simultaneous coexistence of cancer and ESRD, promising longer life. The experience of enzalutamide in HD patients with metastatic CRPC is also among the treatments that have recently appeared in the literature.

In this case, when the docetaxel treatment was started, PSA surge was detected until the third cycle. This increase was evaluated as flare phenomenon. There are studies showing that the cell cycle kinetics of the prostate, the release of PSA from lytic tumor cells, and the low proliferation rate of prostate cancer are related (2).

Docetaxel can be used without dose adjustment in ESRD. However, tubular nephrotoxicity has been reported even in those with normal kidney functions. Takimoto et al. investigated docetaxel-induced tubular nephropathy in 7 patients. Tubular markers were measured after chemotherapy. It has been found to be elevated as in cisplatin-induced tubulopathy (3). AFFIRM study showed that enzalutamide increases the median survival of 4.8 months and a 37% risk reduction in death compared to placebo in mCRPC (4). Therefore, although its usage of ESRD is limited, we started enzalutamide without dose reduction. The patient was followed closely in terms of cardiac toxicity and hypertension, and no increase in blood pressure was detected.

It was reported that the progression in prostate cancer were associated with elevated PTH. It directly increases human prostate cancer cells. PTH receptors are released from bone metastasis cells and increased mortality (5). In our case, after the HD session was increased to 3 days a week, regression was seen and PSA levels decreased than volatile elevations were appeared.

Tarhan et al. showed that hemodialysis caused elevation in all forms of PSA, but the differences were quite small (6). PSA values may increase by 10% in the post-HD period secondary to the hemoconcentration mechanism. Therefore, obtaining PSA before HD should be considered (7).

One of the case reports presented a patient, followed up with half dose (80mg/day) enzalutamide due to side effects such as skeletal pain and anorexia. They found no correlation between HD sessions and active metabolite levels of enzalutamide (8). Therefore, the treatment was reported as safe in patients undergoing HD.

Simoes et al. preferred 160mg/day treatment and no side effects were reported (9). The treatment is ended 7 months later because of widespread progression. Our case, treated without dose adjustment for 5 years, is the longest enzalutamide experience in a hemodialyzed patient without side effects. The patients who have rapid PSA decrease in the first three months of enzalutamide treatment have a longer overall and progression-free survival (10). Our case supports this observation.

CONCLUSION

Since patients on dialysis have been excluded from clinical trials, data on the efficacy and safety of many oncological treatments in such patients are unclear. In CRPC, there are no series with large numbers of patients on the use of enzalutamide in patients with renal dysfunction, and therefore, it is important and valuable to include long-term responses in the literature, as in our case.

ETHICAL CONSIDERATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Status of Peer-review: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Mottet N, van den Bergh RCN, Briers E, Van den Broeck T, Cumberbatch MG, De Santis M, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer-2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. Eur Urol 2021;79(2):243–62.
2. Seok Han K, Joon Hong S. Exponential Rise in Prostate-Specific Antigen (PSA) during Anti-Androgen Withdrawal Predicts PSA Flare after Docetaxel Chemotherapy in Patients with Castration-Resistant Prostate Cancer. Yonsei Med J 2015;56:368.
3. Takimoto T, Nakabori T, Osa A, Morita S, Terada H, Oseto S, et al. Tubular nephrotoxicity induced by docetaxel in non-small-cell lung cancer patients.
4. Loriot Y, Fizazi K, De Bono JS, Forer D, Hirmand M, Scher HI. Enzalutamide in Castration-Resistant Prostate Cancer Patients With Visceral Disease in the Liver and/or Lung: Outcomes From the Randomized Controlled Phase 3 AFFIRM Trial Running title: Enzalutamide and visceral mets in AFFIRM.
5. Schwartz GG. Prostate Cancer, Serum Parathyroid Hormone, and the Progression of Skeletal Metastases. Cancer Epidemiol Biomarkers Prev 2008;17(3):478–83.
6. Tarhan F, Orçun A, Küçükercan I, Çamursoy N, Kuyumcuoğlu U. Effect of hemodialysis on serum complexed prostate-specific antigen levels. Scand J Urol Nephrol [Internet]. 2007;41(5):382–6.
7. Singh Z, Holt SK, Gore JL, Nyame YA, Wright JL, Schade GR. Aggressive Prostate Cancer at Presentation Following Solid Organ Transplantation. Eur Urol Open Sci. 2022;39:79–82.
8. van Nuland M, Groenland S, Bergman AM, Rotmans JI, Rosing H, Beijnen JH, et al. Plasma Levels of Enzalutamide and Its Main Metabolites in a Patient With Metastatic Castration-resistant Prostate Cancer Undergoing Hemodialysis. Clin Genitourin Cancer. 2019;17(2):e383–6.
9. Simões J, Augusto I, Meireles S, Vendeira L, Silva C. Metastatic castration-resistant prostate cancer and the challenge of a patient with chronic kidney disease in hemodialysis. 2018; Available from: http://dx.doi.org/10.4322/acr.2018.011
10. Armstrong AJ, Lin P, Higano CS, Iversen P, Sternberg CN, Tombal B, et al. Prognostic Association of Prostate-specific Antigen Decline with Clinical Outcomes in Men with Metastatic Castration-resistant Prostate Cancer Treated with Enzalutamide in a Randomized Clinical Trial. Eur Urol Oncol. 2019;2(6):677–84.